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MULTIPLE SUPERFICIAL BENIGN EPITHELIOMA OF THE SKIN

ITS DIFFERENTIATION FROM KINDRED AND SIMILAR ERUPTIONS *

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Opinions are divided with respect to certain dermatoses associated with a form of atypical epithelial proliferation to which the name "dyskeratosis" was given by Darier in 1914. This dyskeratosis is observed in Bowen's, Paget's and Darier's diseases, in chronic roentgen-ray and radium dermatitis, in molluscum contagiosum, in senile keratoderma, in xeroderma pigmentosum and occasionally in various types of epithelioma of the skin.

While Paget's disease of the nipple has long been regarded as a clinical and histologic entity, the identity of Bowen's precancerous dermatosis and of extramammary Paget's disease is often predicated on vague and indeterminate clinical and microscopic observations.

DIAGNOSTIC ERRORS

A number of cases appearing in the literature under such designations, as Bowen's disease, the Bowen type of epithelioma and extramammary Paget's disease, are in reality examples of peculiar forms of epithelioma, usually of the basal cell variety, but at times prickle cell and more rarely of the mixed, basal and prickle cell variety, of epithelial cell proliferation.

In the past six years, I have had occasion to observe four patients in whom the lesions were designated as Bowen's precancerous dermatosis by my colleagues, but which on more careful examination proved to be varieties of superficial epitheliomas. In another case, in which the condition was erroneously called multiple pagetoid lesions of the skin, further observation revealed multiple keratodermas following the ingestion of arsenic many years prior to the appearance of the lesions on the skin. In this patient, one of the lesions on microscopic examination, presented the characteristic features of prickle cell epithelioma with dyskeratotic alterations in the rete cells.

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MULTIPLE, BENIGN, SUPERFICIAL, FLAT EPITHELIOMAS

My aim in this paper is to call attention to the condition to which Arning, in 1922, originally bestowed the name " carcinoide," and which Little described as erythematoid benign epithelioma in the following year. It is a disease which many dermatologists have observed in past years and which has long been recognized in this country, under the

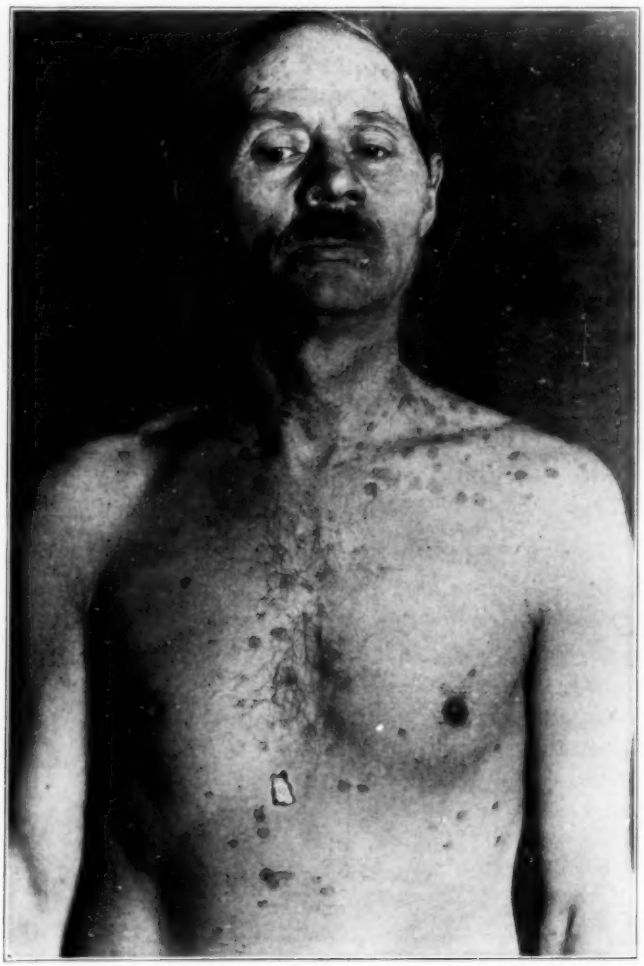

Fig. 1.—Multiple, superficial, flat epitheliomas.

name, multiple, benign, superficial, flat epithelioma of the skin. Because of the occasional incidence of dyskeratotic changes in some of the lesions, the erroneous diagnosis of Bowen's or of extramammary Paget's disease has frequently been made in connection with these dermatoses. At a meeting of the Berlin Dermatological Society held in March, 1918, Jadassohn first suggested that the disease should be considered a separate

group of cutaneous neoplasms. Some instances of multiple, superficial flat epitheliomas are shown in figures 1, 2, 3 and 4.

The eruption differs from other and better known forms of multiple epithelioma in that the lesions are essentially primary multiple formations which develop and have their origin on normal skin; that is, they are not preceded by moles, warts, keratoses, arsenical keratodermas, or by any other so-called precancerous manifestations of the skin. The

Fig. 2.—Multiple, superficial, flat epitheliomas.

lesions in the great majority of the cases are of the basocellular variety; occasionally the prickle cell type is encountered, and still more rarely, a mixed—basal and prickle cell—form of proliferation is demonstrated with the microscope.

Instances presenting all three types in the same eruption have been recorded. In one of my patients, a man, aged 55, there were twelve widely scattered lesions which clinically appeared to be superficial basal

cell growths, and two patches which suddenly took on a rapid growth. Histologically, the latter proved to be prickle cell epitheliomas. The patient died of metastatic carcinoma of the lumbar spine. Jadassohn [1] demonstrated a section from a case of roentgen-ray carcinoma, which showed the histologic features of Bowen's disease in one area of the section, an adjacent area of basal cell epithelioma, and a third field

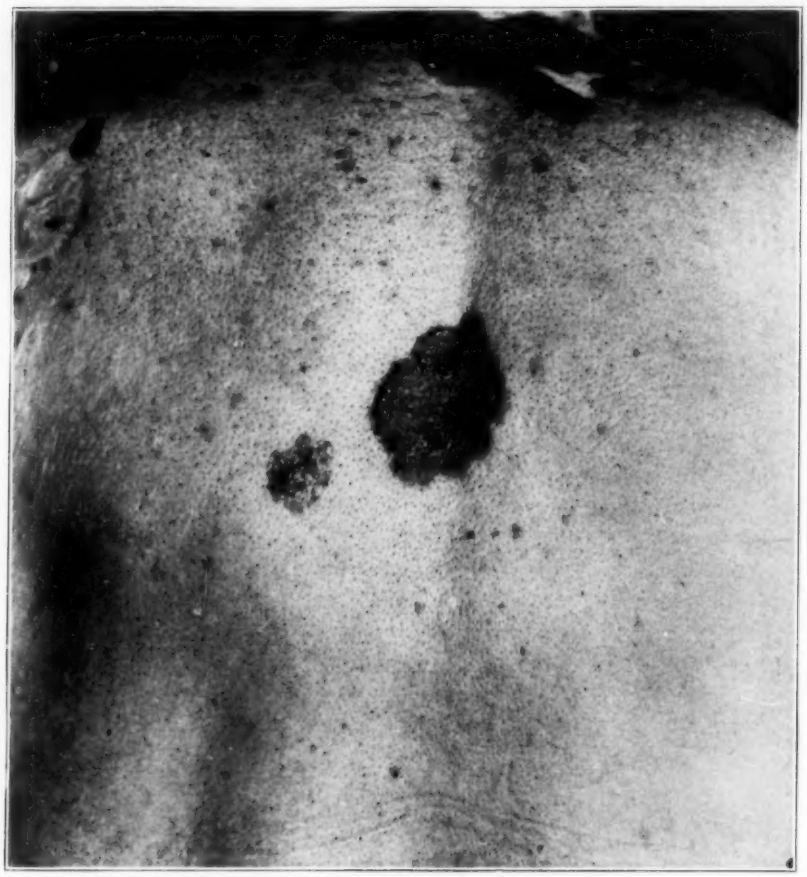

Fig. 3.—Multiple, superficial, flat epitheliomas.

in the same specimen, presented a peculiar adenoid formation which Jadassohn was unable to classify, but which was suggestive of sweat gland epithelioma. A specimen of mixed cell epithelioma, from a case of multiple, primary, superficial epithelioma of the skin, was recently described by Fuss.[2]

1. Jadassohn: Demonstration of Rare Cases of Epitheliomas, Bruns Beiträge zur klin. Chir., vol. 136, p. 2.

2. Fuss, S.: Flaches, oberflaechliches Hautepitheliom, mit eigenartigen histologischen Befunden, Arch. f. Dermat. u. Syph. **153**:1, 75, 1927.

Sequeira's case of "multiple carcinoma of the skin: precancerous dermatosis of Bowen" presented basal and prickle cell epitheliomas and "precancerous" horny papillomas, which despite the marked dyskeratosis of the rete cells cannot be identified with Bowen's disease. The case which Trimble presented before the New York Dermatological Society

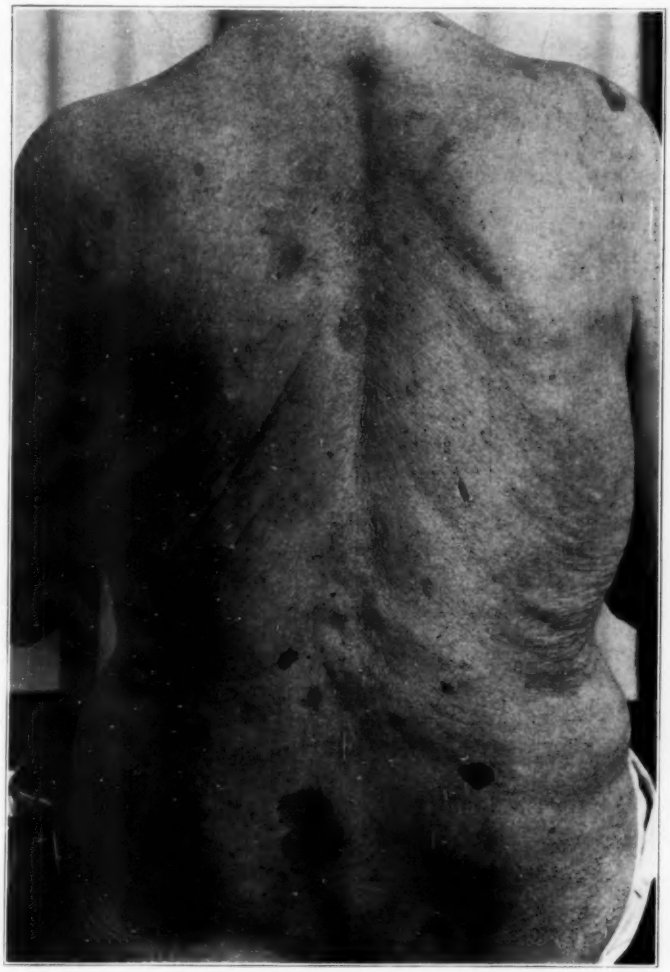

Fig. 4.—Multiple, superficial, flat epitheliomas.

in 1923, in which he called the lesion Paget's disease of the abdominal skin, was histologically a basal cell epithelioma with dyskeratotic changes in the epithelium. A flat basal cell epithelioma is shown in figure 5.

The cases of Morrow and Lee, Mount, Martinotti, and a number of other examples which could be cited, belong in the category of

basal and prickle cell epitheliomas, as has been pointed out by Savatard and other recent writers.

One of Ketron's cases, the report of which he published in a paper in 1919, was an example of multiple superficial epithelioma, but to Little belongs the credit of being the first to publish, in 1923, an account of a group of cases with eruptions to which he gave the name "erythematoid benign epithelioma." He said: "I hope to justify the title I have chosen, and to substantiate the claim that the group is really a new one, not previously coordinated or described." Without wishing in the slightest degree to minimize the significance of Little's

Fig. 5.—Flat, basal cell epithelioma.

publication or to detract an iota from its scientific value, I do not hesitate to say that the dermatosis under discussion had been recognized for many years prior to 1923, by men with whom I have had frequent contact in clinics and medical meetings, such as the elder Fox, Fordyce, Whitehouse and others; we called the eruption, multiple, benign, superficial, flat epitheliomas. The clinical and histologic features of these lesions of the trunk and extremities are in every way identical with those so clearly and succinctly recorded by Little.

CLINICAL FEATURES

As Little has observed, the disease is somewhat more frequent in females than in males. It is seen most commonly in persons between the third and sixth decades of life, but, owing to the fact that the

evolution and course of the eruption is exceedingly slow and insidious, it is probable that the lesions in some of the reported cases began at ages varying between 20 and 40 years. Subjective symptoms, with the exception of slight itching, are usually lacking, and the patient's general health remains unaffected.

The mature eruption appears in the form of multiple red and violaceous discoid patches, either level with or slightly depressed below the surrounding skin, and occurs chiefly on the chest, back and abdomen. The lesions may vary in size from that of a lentil to areas from 6 to 8 or more inches (15.2 to 20.3 cm.) in diameter. Most of them are round, some are oval or have irregular, polycyclic borders. The number of individual lesions may vary from 5 or 10 to as many as 100 (Little's case 2) or more. The face and scalp are sometimes attacked, and in the patients who have many lesions on the trunk, the upper and lower extremities are also apt to be implicated.

The individual lesions make their appearance on normal skin, in the form of flat, shiny macules and slightly indurated papules, of about the size of a large milium body so common on the face. Most of them are light yellow, others have a pale red tint. These macules and papules enlarge peripherally and by the apposition and coalescence of individual lesions, they form lenticular and nummular, usually sharply defined plaques. Some of the mature lesions simulate the ordinary rodent ulcer; others resemble closely an area of chronic dry eczema; occasional lesions have been mistaken for psoriasis; a lesion in one of Little's cases was mistaken for lupus erythematosus by several competent dermatologists.

Most of the patches are devoid of infiltration, and their surfaces are smooth; some of the long-standing lesions impart a sense of resistance to the palpating finger. Slight scaling may occur in some; occasionally, a more advanced hyperkeratosis is observed in one or more of the older plaques. Lesions with crust formation and an underlying oozing surface, thus simulating Paget's disease, have been described. In the mature plaques, the color varies from light yellow to dark brown, and the surface has often a dull, glistening luster.

In many patients, several or many lesions exhibit distinct evidences of spontaneous involution, with a corresponding terminal atrophy of the the surface of the plaque.

The significant feature of most of the mature and more well defined patches is the edge of the lesion, which consists of a narrow, ribbon-like, waxy-looking, barely palpable elevation, similar to but much more delicate than the edge forming the boundary of an ordinary rodent ulcer. In many of the plaques, this waxy line is not discernible unless the skin is stretched. Some lesions have a number of fine telangiectatic vessels shining through the thinned epidermis. Sometimes the process of involution with its accompanying central atrophy results in the

formation of circinate lesions with pale, waxy interiors and reddish to violaceous borders, which resemble the lesions of circinate atrophic lichen planus.

A few instances have been described in which these ordinarily benign lesions had undergone central erosion and ulceration. Fordyce reported a case in which a fungoid proliferation ensued, developing into a malignant tumor.

The essentially benign character of the disease in the majority of cases is evidenced by the absence of glandular metastases, the

Fig. 6.—Bowen's dermatosis.

absence of constitutional disturbances, the extremely chronic and insidious evolution and course and the occasional occurrence of spontaneous involution of the individual plaques.

With regard to its pathogenesis, most writers favor the theory of a congenital predisposition of the skin in the patients, and these authors classify the disease among the nevoid dermatoses.

Arning's designation "carcinoide," was suggested (as Fuhs [3] has pointed out) because of analogous lesions which occur in the mucosae

3. Fuhs, Herbert: Ueber die multiplen Carcinoide der Haut, Acta derm.-venereol. **7**:2, 253 (June) 1926.

of the appendix and the small intestine, and are called carcinoids of the intestines. These lesions, while usually benign, may at times undergo carcinomatous changes, in the same way as those of the cutaneous surface.

A new clinical variety of the dermatosis was recently described by Carol,[4] of Amsterdam, under the name, carcinosis cutis multiformis verrucosa. This article contains a comprehensive review of the subject and also deals with the relationship between the dermatosis and Bowen's disease and Paget's disease.

DIFFERENTIAL DIAGNOSIS

So much has been published about Bowen's disease and extramammary Paget's disease that one need only to confine himself to a brief consideration of the salient features of differentiation from dermatoses which simulate them and which have been mistaken for them. A typical Bowen's dermatosis is seen in figure 6.

The publications of Bowen and Darier are often quoted and well known. More recent pertinent articles have been written by Morrow and Lee, Highman, Ketron, Mount, Little, Sequeira, Savatard, McLeod, Artzt, Biach, Kren, Delbanco, Fuss, Godinho, H. Fuhs, Carol, Martinotti, Pautrier, Ducrey, Muir, Fraser [5] and many others.

A study of the various dermatoses associated with dyskeratotic changes and dealing especially with the histologic aspects, is the subject of a paper by Fraser, presented at this year's meeting of the American Dermatological Association.

A description of Bowen's original two cases, abstracted in his paper of 1912, was worded as follows:

> In both of these cases the patients were males in the fifth decade of their lives. In the first case, the affection had had its beginning nineteen years previous to the time when the patient was first seen; in the second case, four or five years. The lesions were circumscribed; in one case limited to the left gluteal region, in the other to the calf of the right leg. They appeared as papular and nodular lesions, only slightly elevated above the normal skin, of a moderately firm consistency, and dull red in color. The surface was in some places slightly crusted; in other places it had a papillomatous character. The lesions were in places confluent, forming areas of tumor-like masses; in other places, especially at the edge of the affected areas, they were discrete or assumed annular or serpiginous figures. Apparently the lesions never disappeared spontaneously. New lesions slowly grew at the periphery of the areas that had been treated by the curet or by freezing, and there

4. Carol, W. L. L.: Ueber Carcinosis cutis multiformis (verrucosa), Arch. f. Dermat. u. Syph. **152:**705, 1926.

5. Fraser, J. F.: Bowen's Disease and Paget's Disease of the Nipple: Their Relation to Dyskeratosis, Read at the Fifty-First Annual Meeting of the American Dermatological Association, May 1, 1928, to be published.

were apparently some recurrences in the cicatrix or within its boundaries. The subjective symptoms were slight.

Histologically, the lesions showed a marked proliferation of the rete Malpighii in every lesion excised. There were very numerous evidences of karyokinetic division and amitosis, with peculiar clumping of the nuclei and vacuolization of the cells. In the more advanced lesions there was hypertrophy of the horny layer, an hyperkeratosis and parakeratosis, with abundant evidence of cells not having undergone the process of cornification, but showing nuclei surrounded by "membranes" or clear spaces. An edema of all epidermal layers was in the more advanced lesions apparent, which was sometimes so pronounced that a crust was formed at the surface.

The changes in the corium were very constant and in direct proportion to those of the epidermis. In the youngest lesion obtainable, that from case 2, the epithelial proliferation, mitosis, "clumping" of nuclei and vacuolization, were accompanied by enlargements of the vessels in the upper cutaneous layers, which were surrounded by cell masses, of which a large proportion were of the type of plasma cells. In the deeper and more advanced lesions of both cases, the enlargement of the cutaneous vessels was very pronounced and in some places the masses of cells about the vessels were very dense and made up entirely of plasma cells. There was either an absence or great diminution in the elastic fibers in the corium of the affected territory.

Clinically the cases were most puzzling in their appearances, and the upholding of a diagnosis was a matter of much embarrassment. Apart from the course, showing great chronicity as especially emphasized in the first case, the appearance might perhaps suggest late manifestations of syphilis. . . . In the case in question the process had first appeared twenty years previously and had always remained in the same circumscribed territory, the fresh appearances always showing themselves within the area previously affected, or at its edges.

Discussing his cases in detail, Bowen submits his views regarding various aspects of differential diagnosis in relation to Paget's disease of the nipple and extramammary regions, roentgen-ray dermatitis, xeroderma pigmentosum, keratosis senilis, arsenical keratosis and other dermatoses with dyskeratotic changes.

It should be noted that the lesions in Bowen's first two cases were confined to a restricted area of the body—"had always remained in the same circumscribed territory"—as Bowen said; in one the lesion was on the buttock, in the other on the calf of the leg. In Bowen's sixth case, published in 1915, he describes a patient with a dozen or more lesions scattered on the trunk, front and back. The lesions were of thirty years' duration. The largest of these lesions was on the chest, and a section from it revealed a typical epithelioma; the other lesions were relegated to the group of "precancerous dermatosis." A similar case was described by Darier in 1914, as an example of Bowen's disease, in a man, aged 65, who presented three different types of lesions: (1) an epithelioma of the forearm of six months' duration, situated on a large cicatricial surface; (2) papulosquamous lenticular lesions scattered over the same cicatricial surface; these lesions had existed for forty years, and it was their recent transformation that

had given rise to the ulcer, and (3) a malignant right axillary lymph gland. In the light of a broader knowledge of the subject attained in the past fifteen years, these two cases appear to be examples of multiple disseminated epitheliomas, rather than Bowen's precancerous dermatosis. Several competent observers concur with this view; they do not agree with the conception that the different hyperkeratotic lesions described by Darier should either on clinical or histologic grounds be identified with Bowen's lesions. They regard them as simply being associated with such in the same patient.

DIFFERENTIAL DIAGNOSIS OF EARLY BASAL CELL EPITHELIOMA AND BOWEN'S DISEASE

The resemblance between certain forms of superficial, basal cell epitheliomas and Bowen's disease are so close that a clinical differentiation is difficult. If any clinical differences do exist, they are due chiefly to a difference in the anatomic structure of the two types of lesions, manifested by the presence or absence of acanthosis. In early basocellular epithelioma acanthosis is absent, in Bowen's disease it is present. Thus, an early epithelioma is more flat, the color is lighter and of a pinkish tint owing to the thinness of the epidermis and the rarefaction of the connective tissue, and the consistency is softer. In Bowen's disease, because of the acanthosis, the lesion is apt to be more elevated, the color darker and the consistency firmer. These clinical differences are too vague and too variable to be of any practical value.

On the other hand, there are distinct and outstanding differences in microscopic structure. In early basocellular epithelioma, the epidermis is never hypertrophied; there is an absence of edema and acanthosis. There is a moderate proliferation of basal cells, which forms from two to five rows of such cells and goes on to the development of projecting buds of varying size and extent. The cutis below these epidermic changes is rarefied (reticular metamorphosis), stains with difficulty, and in rare instances shows basophilic degeneration. The inflammatory reaction in the corium depends on the rapidity of the epidermic changes. If the latter are extremely slow, there may be little, if any, inflammatory reaction; if rapid, there is an infiltration of a varying number of lymphocytes and plasma cells in the corium. Basal cell epitheliomas, with epithelial budding, are shown in figures 7 and 8.

The microscopic changes in the early stages may be manifested by two modes of development: in one, there is a multicentric epithelial proliferation, which may occur in different regions of the same section, the cell masses protrude down from the basal cell layer as well defined buds and extend into the corium in the shape of strands and papillary formations. In the other mode of development, the proliferation occurs

within the epidermis, in the form of sharply defined groups of cells with dark nuclei (intra-epidermal development of Jadassohn). The epithelial bands and nests are composed of small cuboidal, oval or round cells with a narrow zone of protoplasm and sharply defined nuclei rich in protoplasm. Beneath these epidermal changes, the infiltration in the corium consists of lymphocytes and plasma cells, usually arranged around the blood vessels.

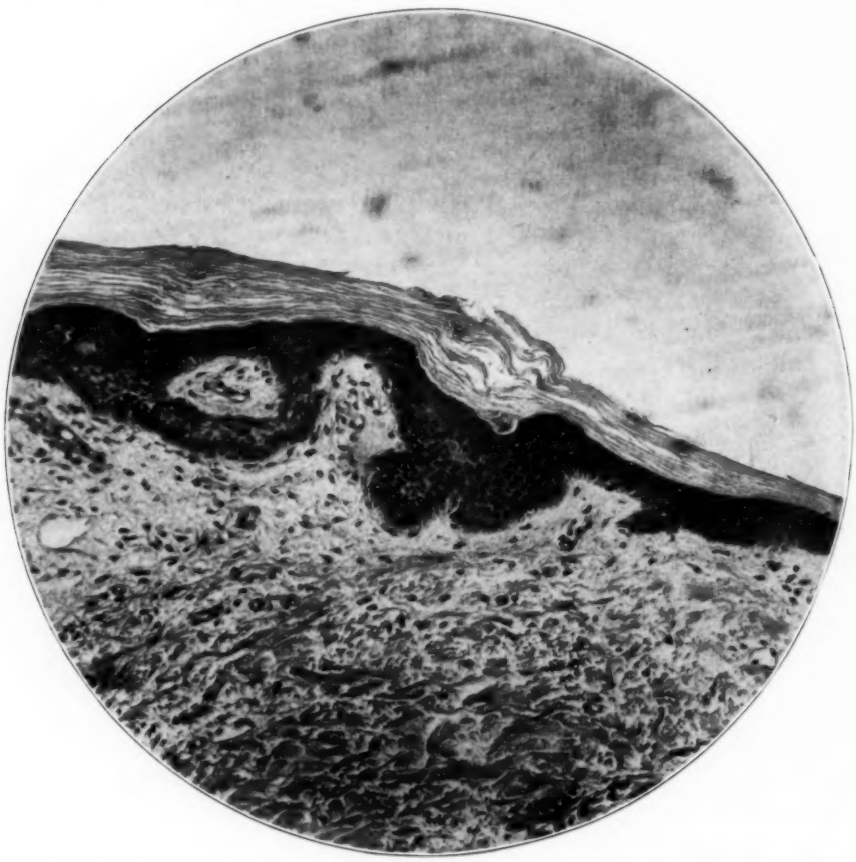

Fig. 7.—Multiple, superficial, flat epithelioma; early basal cell epithelioma, with epithelial budding.

MICROSCOPIC CHANGES IN BOWEN'S DISEASE

In Bowen's disease, the epidermis undergoes a cellular proliferation showing malignant changes, manifested by irregularity in size and shape of the cells, mitotic figures, hyperchromatism and clumping of the nuclei; these alterations—dyskeratosis—occur in the rete layer, together with thickening and proliferation of the pegs, and result in acanthosis. That this dyskeratosis is not a primary but a secondary

change in Bowen's disease is the opinion expressed by Fraser in his recent contribution to the subject. The dyskeratotic cells have irregular, enlarged and deformed nuclei—the "clumped" cells of Bowen. There is also a varying degree of hyperkeratosis and parakeratosis, sometimes absent in certain areas of a given section. In the acanthotic rete layer there is usually a striking multiformity of cellular structure, the cell bodies and nuclei have irregular and distorted shapes as compared to

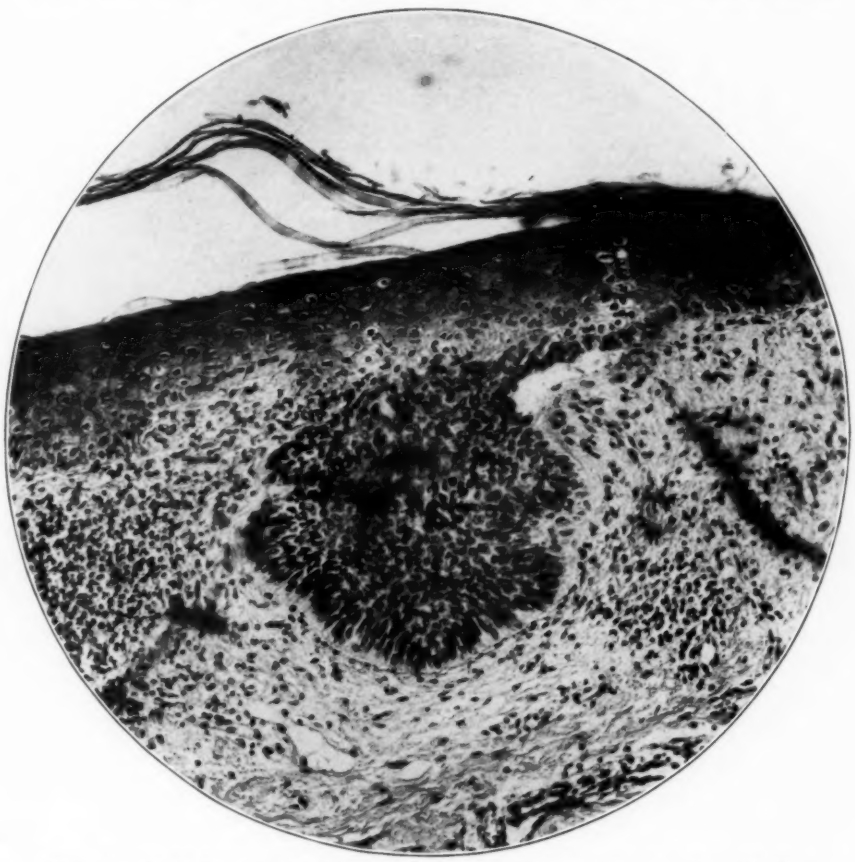

Fig. 8.—Multiple, superficial, flat epithelioma; early basal cell epithelioma, showing more advanced process than the epithelioma in figure 7.

normal epithelium. In the prickle cell layer there is usually considerable intercellular and intracellular edema, with many vacuolated cells and nuclei rich in chromatin. Giant cells of various shapes, enlarged nuclei and multinucleated cells are often seen. The cells contain mitotic figures with irregular and sometimes bipolar chromatin masses. The chromosomes are often "clumped." Some of the multinucleated giant cells are of great size. The palisade arrangement of the basal cell

layer may be distorted or it may remain intact, but there is not any epithelial proliferation or downward budding of masses of cells towards the corium. In the upper portion of the corium, there is an infiltration of cells consisting largely of lymphocytes and plasma cells, together with a few mast cells. The blood and lymph vessels are dilated, and the elastic tissue is diminished. Bowen's dermatosis, with a characteristic dyskeratosis in the epidermis is shown in figures 9 and 10.

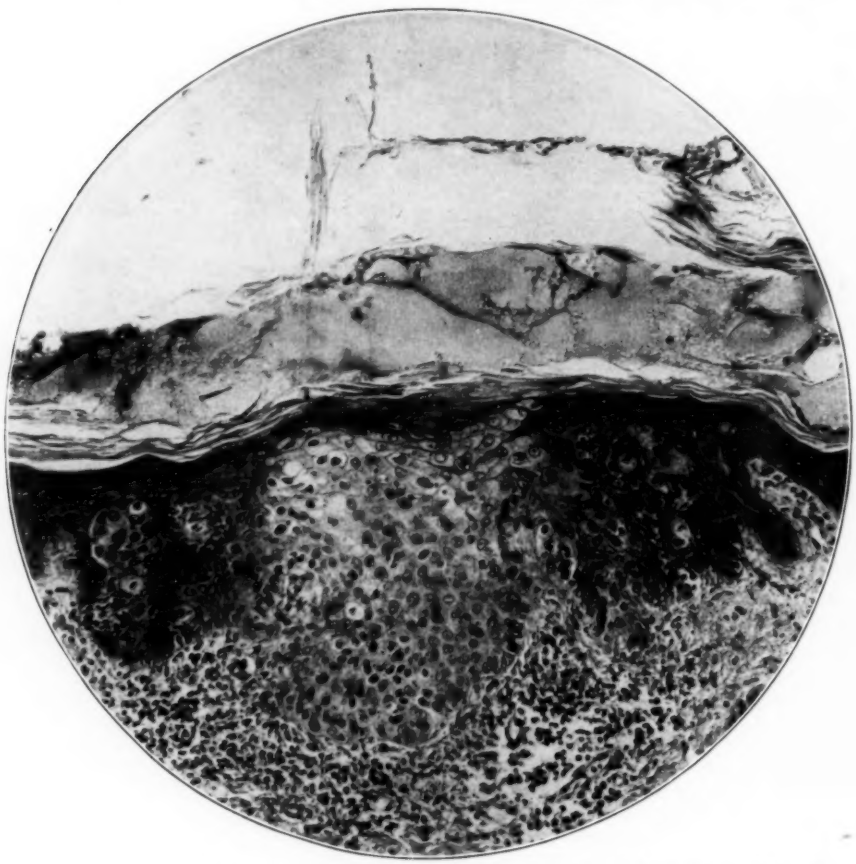

Fig. 9.—Bowen's dermatosis, with characteristic dyskeratosis in the epidermis; early stage.

The structural changes in Bowen's disease may be interpreted as those of an intra-epidermic carcinoma.

In discussing differential diagnosis, Artzt and Biach point out that two criteria should be given consideration in the diagnosis of Bowen's disease: (1) the establishment of histologic diagnosis; (2) the absence of metastases in the glands and internal organs. In their opinion, a definite diagnosis cannot be made on clinical evidence alone. If

Bowen's disease is regarded as a precancerous dermatosis, the incidence of metastases cannot logically be correlated with such a designation; for a metastasis in relation to a new growth of epithelial nature is characteristic of malignant changes and evidence of a true cancerous process. Up to 1925, only twelve of the thirty-four cases reported as Bowen's disease had stood the "acid test" of clinical and histologic scrutiny.

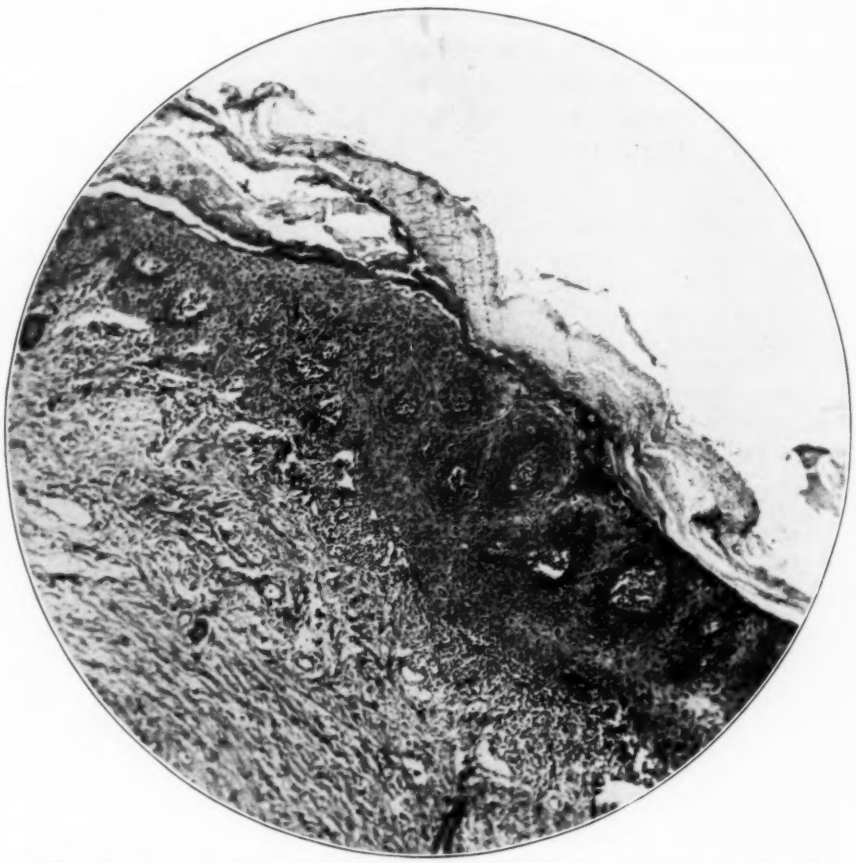

Fig. 10.—Bowen's dermatosis, with characteristic dyskeratosis in the epidermis; more advanced stage than the process in figure 9.

DIFFERENTIAL DIAGNOSIS OF BOWEN'S DISEASE AND EXTRAMAMMARY PAGET'S DISEASE

It is the consensus of opinion that a definite differentiation between Bowen's and extramammary Paget's disease must be based almost entirely on the microscopic observations in each disease. Clinically, it is only in the classic examples that definite morphologic differences may be discerned. Extramammary Paget's disease is always an isolated

lesion, constituting a single efflorescence, while Bowen's disease might be an isolated patch composed usually of multiple lesions, often in various stages of evolution, or it may appear as a disseminated eruption, as did the cases of Artzt and Biach, Godinho and others. Most of the cases appearing in the literature under the designation "pagetoid lesions of the skin" are in reality examples of basocellular or mixed varieties of superficial epithelioma.

Fordyce's case of extramammary Paget's disease might be described as clinically typical except that it lacked the pronounced crust formation and the characteristic oozing of the surface after removal of the crust. Microscopic examination proved it to be a rodent ulcer. It was a single lesion, situated on the left buttock, that bled on slight provocation. He described it as follows:

> An irregularly rounded, flat, dark red lesion involving an area about three inches in diameter. The margin was somewhat polycyclic in outline and was sharply defined against the normal skin. It showed the faintest trace of an elevated rolled edge. The lesion was dry and showed slight epidermic exfoliation, with the exception of a portion, three-quarters of an inch wide in the center, which was eroded, nodular and bled on slight irritation. In its color, general appearance and slow eccentric progression it was strikingly similar to the usual type of Paget's disease of the nipple, and had it been in that location, few would have hesitated to give it that name.

The cases of extramammary Paget's disease so far reported have the same clinical appearance and the microscopic changes as those noted in Paget's disease of the nipple. The differential features are thus the same. There is not a doubt, in Ducrey's opinion, that some of the cases reported in the past may have been cases of Bowen's dermatosis mistakenly diagnosed as extramammary Paget's disease, since it is only recently that the various authors have had their attention called to the latter disease, and the diagnostic problems involved have presented themselves. Several writers have expressed the belief that most cases of so-called extramammary Paget's disease are probably Bowen's disease; Bloch,[6] on the other hand, considers it to be a definite entity.

The importance of microscopic observations in Paget's disease was emphasized by Fordyce when he said:

> Many multiple epitheliomata in the early stages closely resemble Paget's disease. They present all grades, from pale and red scaling patches the size of a split pea or smaller, to patches as large as the hand. They have sharply defined, scalloped margins showing very slight tendency to elevated or pearly rolled edge. Some of them maintain their red and scaling appearance and others become the sites of fungating growths.

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6. Bloch, Bruno: Personal communication to the author.

Thus it becomes evident that the diagnosis of both Bowen's disease and extramammary Paget's disease must be determined chiefly by the microscopic observations.

As to the arsenical keratodermas and arsenical epitheliomas, I have encountered two instances in which the multiple lesions strongly simulated those described in multiple benign epithelioma, Bowen's and Paget's diseases; here again, microscopic examination is of paramount importance, and the patient's history of arsenical medication at once points toward the suspected etiologic factor. The histologic changes were studied and described by Fordyce.[7]

SUMMARY AND CONCLUSIONS

The disease designated by Little as erythematoid benign epithelioma, in 1923, has for many years been recognized in this country under the name, multiple, benign, superficial epithelioma of the skin.

The lesions are usually basocellular new growths, arising primarily on unchanged skin; they may also be prickle cell lesions or mixed cell growths.

Lesions of this kind have been confused with those of Bowen's disease, extramammary Paget's disease and (more rarely) arsenical epitheliomas and keratodermas.

Microscopic evidence proves Bowen's disease to be a distinct entity, with histologic features peculiar to itself, and indicative of intra-epidermic carcinoma; however, the exact status of extramammary Paget's disease is still undetermined, both clinically and histologically.

Although the clinical diagnosis of multiple, benign, superficial epithelioma is usually not attended with any difficulties, it is emphasized that its differentiation from Bowen's and extramammary Paget's diseases, arsenical keratodermas and other lesions which closely simulate the multiple new growths, must be determined largely by microscopic examination of the lesions.

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ABSTRACT OF DISCUSSION

DR. FRASER, New York: I agree with Dr. Wise in regard to diagnostic errors. Probably more than half of the cases that have been reported as Bowen's disease or so-called extramammary Paget's disease have undoubtedly been the type of epithelioma described by Dr. Wise. Dr. Wise's concise and cleancut picture of the clinical features and the histologic differences between these different diseases have been so well defined, that there cannot be any justification for repetition of the diagnostic errors of the past. Reference has been made to my interpretation of the term dyskeratosis. Dyskeratosis simply means an abnormal keratosis, a disorder of keratinization. The phenomenon is not characteristic of either Paget's

7. Fordyce, quoted by Bowen: Precancerous Dermatoses, J. Cutan. Dis. **30**: 241, 1912.

or Bowen's disease. It may occur in any condition resulting from epithelial irritation, whether neoplastic or inflammatory. I do not see any reason, therefore, for characterizing either Paget's or Bowen's disease as dyskeratosis. The primary histologic picture of Bowen's disease is anaplasia and not dyskeratosis, which is a secondary and unimportant phenomenon. I have seen as much dyskeratosis in roentgen-ray cancer as I have ever observed in Bowen's disease.

The question of the occurrence of extramammary Paget's disease has been left open by Dr. Wise; whether wisely or unwisely, time will tell. I am one of the recent writers referred to by Dr. Wise, who believe that many of the cases reported as extramammary Paget's disease were either Bowen's disease or basal cell epithelioma. It is true that lesions have been described on the abdomen and other parts of the body which presented all the clinical features of Paget's disease of the nipple. Cheatle has recently reported such a case, which he characterized as Paget's disease of the nipple on the abdomen. Muir examined a section in this case microscopically and thought that the cells resembled those of a rodent ulcer. So keen an observer as the late Dr. Fordyce reported two cases of extramammary lesions with all the clinical features of Paget's disease of the nipple, but these cases turned out to be basal cell epithelioma. A case which came under my observation and was reported as Paget's disease of the abdominal wall was histologically a case of Bowen's disease. The whole question of whether Paget's disease ever occurs in other regions than the nipple can be settled only when there is universal agreement as to what is really meant by Paget's disease. We must establish a constant. If we accept the view that Paget's disease is a primary lesion of the epidermis, taking its origin from epidermal cells, we can conceive of extramammary Paget's disease. The balance of the evidence seems to be against this conception. Morphologically, the Paget cells are larger than prickle cells and to my mind resemble far more the columnar cells of the lactiferous ducts.

If, on the other hand, Paget's disease is due to extension upward from a duct cancer, and this I think is the view accepted by the majority of modern investigators, then the idea of Paget's disease in any other situation than the nipple is inconceivable unless we postulate the existence, first, of supernumerary nipples or second, an epidermal lesion secondary to a cancer of sweat ducts. I have not encountered either of these conditions.

DR. MONTGOMERY, Rochester, Minn.: I have been interested in this subject and recently have studied fifteen cases. I agree with Dr. Wise and Dr. Fraser, but wish to add a few points. Frequently these superficial epitheliomas start as single lesions. This occurred in six of my series of fifteen cases. The dry, erythematous, scaling plaques with a threadlike elevated border, as described by Little under the title of erythematoid benign epithelioma, microscopically are usually basal cell epitheliomas. The crusted eczematoid patches and the fungating tumors developing in the center of erythematoid plaques are usually squamous cell epitheliomas. I have one patient showing basal cell epithelioma, basal-squamous cell epithelioma and squamous cell epithelioma (grade III, Broders). Dr. Ormsby's[8] case, reported in the proceedings of the Chicago Dermatological Society, proves that metastases can occur. Two of my fifteen patients had frank squamous cell epitheliomas.

Bowen's disease can be diagnosed only microscopically. However, one can see at times the same microscopic picture that occurs in Bowen's disease in

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8. Ormsby, O. S.: Superficial Epitheliomatosis with Metastases, Arch. Dermat. & Syph. **13**:687 (May) 1926.

roentgen-ray dermatitis and senile keratosis, so that the clinical observations in addition to the microscopic observations are necessary for a definite diagnosis. Whether we accept Bowen's disease as an early epithelioma or not, the microscopic changes are such that it changes into a squamous cell epithelioma rather than into a basal cell epithelioma.

In regard to extramammary Paget's disease, the microscopic picture is apparently that of either a basal cell epithelioma or a squamous cell epithelioma, or, in rare cases, that of Bowen's disease. I have not seen or found a case reported in the literature in which there were typical Paget cells.

Finally, I wish to emphasize the fact that epitheliomas arising from the administration of arsenic in any form should not be confused with the superficial epitheliomas that Dr. Wise has described. Whereas these epitheliomas usually arise from arsenical keratoses on the palms and soles, they can occur on the trunk and resemble the superficial epitheliomas under discussion. Microscopically, however, they are extremely malignant squamous cell epitheliomas, usually resulting in early metastases and death.

DR. MICHELSON, Minneapolis: I think that we should consider carefully the clinical use of the term benign. As Dr. Wise showed, and Dr. Montgomery brought out, these lesions are not all benign. I think that we should use the term, superficial epithelioma of the skin, but that one must make a microscopic examination before one can say whether these lesions are benign or not.

DR. FINNERUD, Chicago: I think that many of us have been misled by Bowen's original illustrations and description into believing that in order to be of the so-called Bowen type, the lesions should have the outline of the tertiary syphilid. I think that one of the valuable points in Dr. Wise's paper is the fact that he has pointed out clearly that a discoid lesion, or one of other than circinate outline, may represent grossly Bowen's disorder.

DR. PUSEY, Chicago: The point I wish to emphasize is that in all of these varieties we are dealing with carcinoma. Not being a fancier or collector of epitheliomas, I am not much interested in the little differentiations that occur between them. For the expert and for the collector it is desirable that these things should be known, but for us of the rank and file it is much more important to get a clear conception of the fact that in all of these epitheliomas we are dealing with the same condition. It may be a Queen Marie tulip or a Queen Wilhelmina tulip, but it is still a tulip, and that is the point to bring out in the discussion of these epitheliomas. I am interested in one or two points about which I do not entirely agree with Dr. Wise. I do not like the term "benign" applied to these multiple, superficial epitheliomas. It might just as well be applied to the rodent ulcer. I have now under observation a case which I had Dr. Fox demonstrate at one of our meetings some years ago. The lesions have remained in the same spot for several years, but they are still epitheliomas. They are potentially dangerous, and some of the lesions have progressed further.

In regard to the question of Paget's disease, the first paper I ever wrote was on Paget's disease of the nipple, and, like many authors who enjoy reading their own work occasionally, I read that paper recently and also read Paget's original paper. Paget describes it as a disease beginning in the nipple and extending downward. I have not the slightest doubt, particularly after the report of Dr. Fraser, that there is a process that begins lower down and reaches the nipple; but neither have I any doubt that there is a disease which begins in the areola of the nipple and goes downward, and that disease was the one Paget described.

They are two processes, beginning differently, one like the superficial multiple epithelioma that begins in the nipple, and another that begins in the lactiferous duct.

Another thing that I wish to protest against is the naming these diseases after a person. There are two types of Paget's disease. Take the old rodent ulcer, that goes back to the Old Testament as Jacob's ulcer, and yet we want to call it Krompechers' tumor. I wish to protest against this habit, for it keeps us busy all the time remembering that Jacob's ulcer is rodent ulcer as well as Krompecher ulcer.

Dr. Bechet, New York: This particular type of epithelioma is not uncommon in large clinics. I can readily understand why Dr. Wise uses the word benign in connection with this type of epithelioma, as it frequently is present for many years without any sign of activity; on the other hand, I am heartily in agreement with Dr. Pusey in his objection to the term "benign" as applied to any type of epitheliomatous change. As an example of the misapplication of the term, I can recall a flat cicatricial epithelioma, exactly similar to the lesions described by Dr. Wise, which occurred on the forehead of a woman. It had been present for many years, yet in the center of this flat epithelioma, which was about 6.5 cm. in diameter, was a fungating, cauliflower growth, about 3 cm. at its widest part, which had been growing rapidly. A biopsy proved the fungating growth to be a prickle cell epithelioma, and the flat lesion a basal cell epithelioma. In view of this experience, which is not a unique one, I deem it wise to drop the term benign in connection with any type of epithelioma.

Dr. Ayres, Jr., Los Angeles: I have a case under observation now in which the lesions have practically disappeared as the result of treatment by the roentgen ray. The lesions range in size from that of a pea to that of a palm; they are red, with areas of excoriation, suggesting a chronic eczematous patch, but they have the sharply defined, pearly, ribbon-like, scalloped border. The itching was one of the factors that brought the patient to me for advice.

Dr. Eller, New York: I have seen two cases in which both microscopic pictures were seen in the lesions on the same patient; some were the lesions of Bowen's disease, and the others were typical, flat basal cell epitheliomas of the skin. Both types require the same treatment—large doses of irradiation, either radium or roentgen ray, in the beginning. Small doses do not seem to eradicate them.

Dr. MacKee, New York: We all are in accord with Dr. Pusey's opinion that these lesions are all epitheliomas of slightly different clinical and histologic types. However, it is important, for the purposes of teaching and conversation, to divide them into entities, if possible, even though they are all placed in one group. It seems to be difficult, at present, to differentiate clinically, and even histologically, between Bowen's cancer, extramammary Paget's disease and the various types of cutaneous epitheliomatosis; that is, the flat type of basal cell epithelioma. If my recollection is correct, both Bowen and Darier have been confused, and I think that two of their cases proved to be basal cell epitheliomas. About the only positive differentiation is histologic: Bowen's cancer begins as cancer within the epidermis, while in the case of cutaneous epitheliomatosis, there is a down growth of epidermis, that is, cancer beginning in the derma. It is probable that all these lesions are cancer from the beginning, and that they are placed among the precancerous dermatoses partly for convenience and partly because some of them cannot be classified as cancer according to the present classification, because the extremely early lesion shows only hyperkeratosis, acanthosis, and perhaps dyskeratosis and a little inflammation later. It has been the custom not to classify

such a lesion as cancer until there is a wild growth of epithelium associated with an inflammatory reaction in the derma.

Dr. Wise, New York: The entire concept of the subject can be clarified if we remember the predisposition of the skin and regard the condition as nevoid disease. To prove this possibility of an anlage, a man may have Bowen's disease on one part of the body, a basal cell epithelioma on another and a squamous cell neoplasm on still another. They are all variations of epithelioma in the light of a nevoid disease. Regarding the word benign, tradition has crept in. Some one called the condition that, and the designation has persisted. The term relatively benign would be more appropriate, but is awkward. I agree with Dr. Michelson and others who object to the term on the ground that an epithelioma is not benign; but there is no question in my mind that there are relatively benign epitheliomas, because many patients have lesions, extremely superficial, that have been mistaken for lupus erythematosus, psoriasis, and so on, which are benign in the sense that they have persisted for thirty years or more without any evidence of metastasis or without causing any discomfort to the patient, except from the cosmetic standpoint.

In regard to extramammary Paget's disease, there is a great difference of opinion. I spoke to Bloch, who has done some work in this field, and he is firmly convinced that extramammary Paget's disease does exist and can be differentiated histologically from other lesions of similar nature.

With reference to metastases, there are many recorded cases in which metastases took place from these superficial neoplasms. These have occurred in the viscera as well as in the spine. They have been observed in cases of Bowen's disease, in prickle cell growths and, more rarely, even in basocellular neoplasms. Many of these superficial lesions present a dyskeratosis of the epidermal cells, but they should not all be classified as examples of Bowen's disease.

SKIN DISEASES OF ENDOCRINE ORIGIN (DYSHORMONAL DERMATOSES)

POIKILODERMA-LIKE CHANGES IN CONNECTION WITH UNDERDEVELOPMENT OF THE SEXUAL GLANDS AND DYSTROPHIA ADIPOSOGENITALIS *

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Dermatologists have always shown particular interest in skin diseases the pathogenesis of which is related to the entire organism or to definite changes of the internal organs. Such relationships, either to intermediate metabolism or to disturbances of particular internal organs, have always been sought. The developments of the last few years have shown that the endocrine glands oftenest deserve consideration in this respect. This is entirely comprehensible, for there is no doubt that endocrine functions strongly influence even the normal physiologic development of the skin.

In looking over the tremendous amount of literature which has accumulated through the years in this field, we are, however, astonished to note the preponderance of hypotheses over the relatively few facts. We know that in Addison's disease a hyperpigmentation of the skin and mucous membranes is caused by the destruction of the suprarenal glands. It is also known that a causal relationship exists between insufficiency of the thyroid and myxedema of the skin, and that, especially in women, disturbances of the sexual apparatus can cause eruptions on the skin. Though it is impossible to say which particular gland is primarily affected, such relationships are, moreover, probable in several other skin syndromes; for instance, in scleroderma, in impetigo herpetiformis and in some cases of acanthosis nigricans. However, we know nothing about the internal pathogenic mechanism even in those dermatoses in which the endocrine etiology is beyond doubt, and which I have grouped under the name of dyshormonal dermatoses. Up to the present, it has been impossible to form a correct conception of the ways and means by which disturbances of hormonal functions cause a functional or anatomic change in the skin. The cause for this cannot be attributed to a lack in scientific dermatologic study but to the fact that, in spite of the great amount of research work, the physiology and path-

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* Read by Bruno Bloch at the Fifty-First Meeting of the American Dermatological Association, Washington, D.C., April, 1928.

ology of endocrine glands and their correlations are not yet sufficiently advanced to permit the solution of such problems. Dermatologists must therefore for the present content themselves in collecting casuistic material, that is, they must classify the cases and forms in which the endocrine origin is either certain or at least highly probable. Future research must then disentangle the various threads which join the internal changes with the skin.

This communication is a casuistic contribution of this kind. It concerns a new or formerly not clearly recognized relationship of changes in the skin and endocrine disturbances, which we have observed in two cases.

REPORT OF CASES

As a report of the first case has been published in detail by one of us (Bloch [1]), it will only be necessary to summarize it briefly:

CASE 1.—In a woman, aged 22, without hereditary stigmas, the changes in the skin began in early youth; they were progressive in their course and were of diffuse, almost universal distribution. They consisted of partly diffuse, partly circumscribed atrophy, sometimes of high degree, and of a diffuse network and spots of hyperpigmentation and depigmentation. In some parts, fine telangiectasia occurred. The entire skin was extraordinarily dry. The nails were thin and atrophic. Lanugo hair was entirely absent and the hair of the eyebrows, eyelashes, axillae and mons veneris scarcely developed. This atrophy was also apparent histologically. There were no sweat glands, and the follicular apparatus was atrophied. The teeth were underdeveloped, atrophic and small and the breasts rudimentary. A juvenile cataract of both lenses was further worthy of note. (When she was 5 years of age, an operation for removal of the cataract was performed.)

The composite picture indicated endocrine disturbances as the cause. Though the examination of the hypophysis and the thyroid gave negative results (the basal metabolic rate and the roentgenograms were normal), the examination of the genital organs revealed serious pathologic changes. The pelvis and external genitalia were infantile. The patient had never menstruated and neither uterus, ovaries nor tubes were found.

CASE 2.—*History.*—A peddler, aged 40, did not present any hereditary taint and particularly no signs of syphilis. He was prematurely born and as a child had severe rickets. At the age of 4½ years he was operated on for juvenile cataract of both eyes and at 17 had a bilateral ulcerating keratitis. Since this time, his vision has been greatly impaired by the residual maculae. He was always thin and weakly as a child. He had never suffered a serious illness and was not backward in school. Owing to his impaired eyesight, he had been a peddler since he was 20. In his sixteenth year his libido awakened. It was always weak but heterosexual. He never had an ejaculation brought about either by intercourse or spontaneously. His external genitalia was never larger than those

1. Bloch, B.: Ueber Beziehungen zwischen Hautleiden und endokrinenen Störungen, Schweiz. med. Wchnschr. Jahrg. **56**:31, 1926; Ueber die Beziehungen zwischen Hautkrankheiten und Gesamtorganismus, Karlsbader ärztl. Vorträge. Internat. ärztl. Fortbildungskurs, Balneologie and Balneotherapie **9**:478, 1927; Haut und Stoffwechsel, Verhandl. d. Gesellsch. f. Verdauungskr., 1925.

of a small boy. His voice remained unchanged. On account of these conditions and his remarkably small thyroid gland, it was suggested to the patient in 1911 that Professor Kocher should make a thyroid implant. The patient, however, could not decide to undergo this operation. In spite of the fact that as a pedler he was constantly active during the entire day, a remarkable obesity set in in his twenty-fifth year and had existed up to the time of examination. The skin was always extraordinarily dry and scaled easily. The changes of the skin, above all the pigmented spots, began to develop during his childhood. From time to time wheallike lesions on the skin, which itched severely, appeared. His hair, which had always been sparse, began to grow gray at the early age of 25. The

Fig. 1 (case 2).—Appearance of patient.

hair never developed on his face, eyebrows or pubic region. His nails were always bent and furrowed. As early as 1916, the patient came to our clinic on account of a spontaneous hemorrhagic condition in the region of the left trochanter. He came to us again recently on account of an itching eruption on the skin of the lower extremities.

Examination.—The patient was of middle stature and presented a remarkable, almost grotesque appearance. In spite of his childlike face, he looked old for his age. His hair was sparse, both on the crown of the head and in the frontal regions. On the neck and temples it was almost entirely gray. The upper part of the head was small and the face was childlike, with small, deepset eyes and a small,

underdeveloped and flattened nose. The cheeks, the chin and the throat were surrounded by rolls of fat, so that the head seemed to be resting directly on the thorax. The tremendous disproportion in the sizes of the trunk and the extremities was striking. The thorax was broad and barrel shaped, with large rolls of fat. The breasts were like those of a woman and were developed to large pendant mammae. The nipples, on the other hand, were small and insignificant. Large rolls of fat extended from the breasts to the armpits. The fat of the abdomen was also extremely abundant and hung down broadly on both sides. There was a deep fold between the pendant belly and the mons veneris.

Fig. 2 (case 2).—Left knee of patient, showing atrophy, hyperpigmentation, depigmentation and telangiectasias.

The mons veneris was covered by a thick layer of fat. The entire torso impressed one as that of an old and fat woman. In contrast to it, the extremities were strikingly thin, small and dainty. The various members were too short, the fingers almost like stumps. Both muscles and fat of the upper and lower extremities were decidedly underdeveloped. The hands and feet were particularly small. The short, thin extremities did not seem to suit the heavy and thick-set torso, but seemed to have been transfered to it from some other body.

The skin of the scalp was thin and tightly stretched. Over it were scattered numerous sharply demarcated, yellowish-brown, frecklelike pigmented spots, varying from the size of a pinhead to that of a pea. Depigmented spots were also

present. The skin of the forehead and the chin was greatly wrinkled. Numerous scattered and irregular pigmented spots as well as less numerous depigmented ones were distributed on the face in the same manner as on the scalp. Areas of fine telangiectasia were present in great number on the cheeks, the chin and the throat. Together, they gave these parts a faded red color. The ears were stunted, with only rudimentary lobes and were covered with brown and white spots and numerous telangiectasias. These changes in some places resembled those in lupus erythematosus. The face was devoid of hair. Even the eyebrows were lacking, and the lashes were represented by an occasional small hair. The lips were narrow and atrophic. The skin of the trunk was dry and scaled slightly in places. Numerous brown and white spots were also present over the breast and abdomen. The skin of the thorax was also plainly atrophic, so that the veins could be clearly seen. In certain parts the atrophy was diffuse, in others more circumscribed. Telangiectasia could be clearly seen here as well. Numerous atrophic striae were present over the lower part of the abdomen. These began above the navel and stretched toward the inguinal region. The skin was highly atrophic in the regions above the iliac crest. On the back, particularly in the lumbar region, hyperpigmented and depigmented as well as atrophic areas and isolated areas of telangiectasia were found. The skin of the extremities, especially of their extensor surfaces, was changed in a similar manner, but even more markedly than on the trunk. Here, yellowish to dark brown pigmented spots intermingled with white depigmented ones were found, as well as partly diffuse, partly circumscribed atrophies. Here also we found a few areas of telangiectasia, mainly on the elbows and knees. The backs of the hands were diffusely pigmented. The skin of the extremities also showed a branlike scaliness. There were numerous hyperkeratotic areas on the wrists and on the palms of the hands as well as on the soles of the feet. Those of the palms had peculiar hollows in their centers and those of the feet resembled oyster shells. The feet, the toes and the fingers were short and thickened at their distal ends. The finger and toe nails were markedly altered. Either they were entirely missing, as in the case of the index finger of the right hand, or they were so stunted that only irregularly formed horny scales remained. These were remarkably strongly curved toward the palm at their distal ends. There were no hairs on the trunk and on the extremities; at the pubic regions were a few stunted and straight, not curled, hairs.

The penis was infantile, about 3 cm. long, and little thicker than a lead pencil. The scrotum was about the size of a walnut. The testicles were hardly as large as beans and could be pushed back into the abdomen through the patent inguinal canals. Brown, lentigo-like spots alternating with depigmented ones covered the entire skin of the genitals and the nates.

Some of the teeth showed marked caries and some were of rudimentary development, little stumps without characteristic form. The second incisors and the premolars were missing on both sides. According to the patient's statement, only thirty teeth had developed.

The internal organs, the blood and the urine were entirely normal. Roentgenograms of the bones showed only partial atrophy, a marked narrowing of the terminal phalanx and a thin skull like that of a young child. There were no further abnormalities and particularly no changes of the epiphyses. An atherosclerosis of the small peripheral vessels was also seen roentgenologically.

X-ray pictures showed the pituitary gland to be small. The nasal sinuses were also below normal size. The thyroid gland was small but could still be found. On the left side of the throat there was a compact smooth nodule about the size of a walnut.

The nerve reflexes were normal and the Wassermann reaction negative.

During both periods of hospitalization, the patient's temperature was remarkably low, between 95 and 96 F., whereas his pulse rate was normal.

Histologic Examination.—The biopsy specimen from a region above the right knee showed the following: The horny layer was wider than normal throughout the entire section. The width of the epidermis was irregularly reduced; in some places, only a few cell layers remained. Here the characteristic differentiation was no longer present. The basal cells were irregular and flattened; there was no spinous layer and the boundary line to the cutis was straight. In other

Fig. 3 (case 2).—Histologic picture, showing atrophy of the epidermis, dilated blood vessels and lime deposits in a vessel. OC. 4 Aa_2 (Zeiss).

places the epidermis was broader, the differentiation of the layers was preserved and the rete pegs and their corresponding papillae were seen but had an irregular form and arrangement. In the atrophic places, the pigment was missing, while in the others, especially in the brown spots, it was clearly increased. The sweat glands and follicles were entirely absent. The connective tissue of the cutis was unchanged. The elastic fibers were generally well developed, but in some papilli they were clumped whereas in others only a few were present. In the papilli and in the pars reticularis there were greatly dilated capillaries. At one place in the wall of a blood vessel, there was a deposit of lime.

COMMENT

In comparing the two cases we find nearly identical changes in the skin, which began in early youth, which progressed and which are associated with severe endocrine disturbances.

These changes in the skin occurred in greater degree in the second case, but the resemblance was so strong that their wax models could be mistaken for one another. The changes consisted of alterations in pigment formation and atrophy and dilatation of the blood vessels. In the second case, they were associated with hyperkeratosis on the hands and feet.

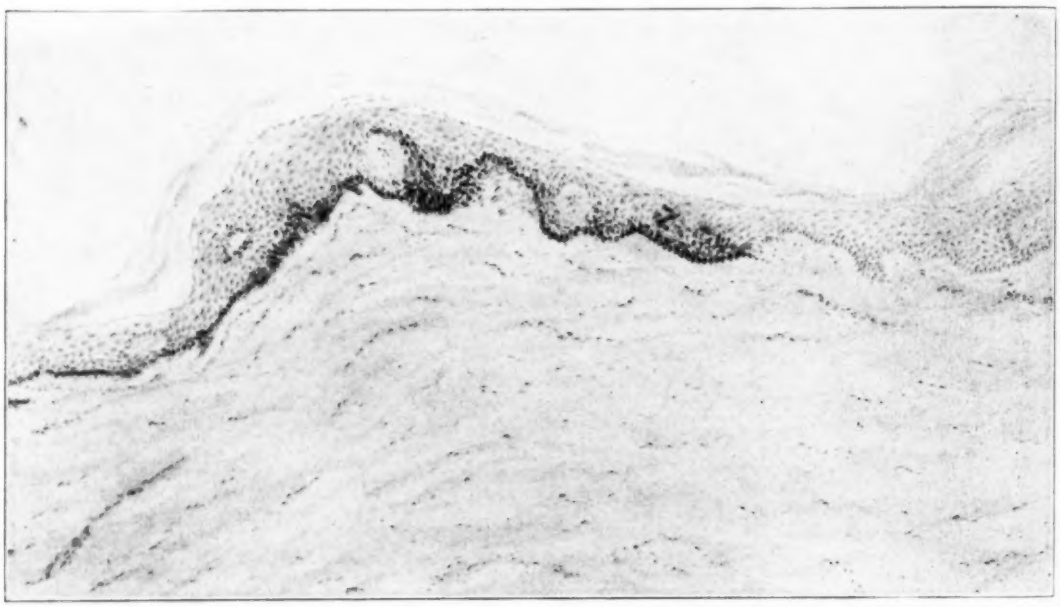

Fig 4 (case 2).—Hyperpigmentation and depigmentation. OC. 4 A, 15 mm. ap.

The hyperpigmentation was the most remarkable change. The face, the extremities, the genitalia and parts of the trunk were covered with somewhat lentigo-like spots and with less numerous depigmented areas which gave the skin an extraordinary spotty, sometimes almost leopard-like, appearance. In the second case, the hair of the head was also strongly depigmented.

Besides the pigmentary changes, marked areas of atrophy were observed. They were in bands and also irregularly distributed areas on the face, breasts and extremities. They were also distinct histologically. Less apparent in the general picture was the telangiectasia, which was found mainly on the extremities and in the second case also

on the face. In contrast with poikiloderma, it was not so pronounced and did not form clearly seen red spots.

The mucous membranes were not affected.

The glands of the skin, the follicular apparatus and the hair were affected to a great degree. In both cases the body hairs, including the pubic hairs and the eyebrows were lacking, and the eyelashes were sparse and stunted. In the second case, the hairs of the head were not fully developed and were mostly gray. The sweat glands were absent in both cases.

The underdevelopment of the teeth in both cases is worthy of note. Some of them were entirely lacking.

The juvenile cataract and the shortness of the most distal phalanges are further worthy of note.

The breasts of the woman were rudimentary, whereas those of the man were extraordinarily strongly developed.

The condition found on histologic examination corresponded to the clinical symptoms. In some parts, the epidermis was hyperpigmented and in others depigmented, and here and there it was plainly atrophic. Several of the capillaries were dilated. There were no marked inflammatory changes and no scleroderma-like or myxedema-like changes. In both cases we found deposits of lime in the wall of the blood vessels and slight changes in the elastic tissue fibers.

The entire picture of the skin already described is characteristic and was extraordinarily similar in both cases. It is, however, difficult or impossible to classify the condition in any one of the known dermatoses.

A classification with poikiloderma atrophicans vascularis which Jacobi [2] first described would perhaps seem the most plausible. However, there are several objections to this; the telangiectasia and also, to some degree, the atrophy are much too slight in comparison with typical cases. As can be seen in the photographs and models, the changes in the pigment are here the most important and, in addition to the dry and atrophic consistence of the skin, stand in the foreground of the clinical picture. Moreover, as Lane [3] showed plainly in his detailed summary of the literature on this subject, the term poikiloderma is not applied to a sharply defined pathologic entity, but rather to a group of variable symptoms. It becomes evident, when one reads the literature on this subject, that different and dissimilar dermatoses have been grouped

2. Jacobi: Jkonograph. dermat., 1906.

3. Lane, J. E.: Poikiloderma Atrophicans Vasculare, with Report of a Case by Oliver S. Ormsby, Arch. Dermat. & Syph. **4**:563 (Nov.) 1921; Poikiloderma Atrophicans Vasculare (Conclusion of Previously Reported Case), Arch. Dermat. & Syph. **8**:373, 1923.

under this name only on account of their superficial resemblances. These diseases are even less an etiologic entity, so that the classification of an individual case in this group means little and does not aid us as regards its pathogenesis. Our cases also differ from Jacobi's type in the high grade regressive changes of the hairs, the nails, the follicular apparatus and the sweat glands. Particularly in conjunction with the anomalies

Fig. 5 (case 1).—Histologic picture, showing atrophy, dilated vessels and lime deposits. OC. 4 A, 15 mm. (Zeiss).

of the teeth and the juvenile cataract, which were present in both cases, do these changes point clearly to the hormonal origin.

And, as a matter of fact, careful examination did bring to light severe changes in the endocrine organs. Both cases showed in common a complete anatomic and functional underdevelopment of the sexual glands as well as of their dependent organs and functions.

In the first case, the internal genital organs were lacking and the outer genitalia were infantile. The patient had never menstruated. In the second case, the testicles were rudimentary and functionally insufficient and the external genitalia infantile. In this case, the pituitary gland was also affected (either primarily or secondarily) and the picture of a classic atrophia adiposogenitalis had ensued. Perhaps the subnormal temperature here is connected with some change in the thyroid gland. Surely further proof is not necessary of the close causal relationship between the changes of the endocrine glands and of the appendages of the skin (hair, nails, sweat glands) as well as of the teeth and the lens in both cases and the remarkable regional development of fat and the childlike voice in the case of the male patient. Experimental results in physiologic embryology as well as in clinical investigations have proved such relationships with absolute certainty.

It is also beyond question that the changes of the skin itself which compose the unusual symptomatic picture, the hyperpigmentation and depigmentation, the atrophy and telangiectasia, have the same endocrine genesis. The coincidence of this unusual group of symptoms of the skin, with the described and seldom observed anomalities of the endocrine glands leads with certainty to such a conclusion. Besides this, we already know that each of the symptoms of the skin which occur in these dermatoses can be the result of endocrine anomalies.

Hyperpigmentations are found in dysfunctions of the suprarenals, in pregnancy, in exophthalmic goiter and in scleroderma.

Atrophic changes of the skin are also often considered as having some relationship to endocrine disturbances; for instance, in scleroderma the atrophy is specially considered as connected with changes of the thyroid (Pollitzer), and in acrodermatitis chronica atrophicans, Pautrier and Eliascheff [4] assumed that thyroid disturbances were present, although Jessner [5] could not confirm this fact. The relationship between striae and pituitary disturbances was stressed by Hermstein,[6] Singer,[7] Volk,[8] Brünauer [9] and Kogoj,[10] and the connection between poikilo-

4. Pautrier, L. M., and Eliascheff, Olga: Contribution à l'étude de la dermatitis chronique atrophicans, Ann. de dermat. et syph. **2**:241, 1921.

5. Jessner, M., and Löwenstamm, A.: Bericht über 616 Fälle von Akrodermatitis chronica atrophicans, Dermat. Wchnschr. **79**:1169, 1924.

6. Hermstein: Striae cutis distensae und Hypophysentumor, Arch. f. Dermat. u. Syph. **146**:360, 1924.

7. Singer, O.: Beiträge zur Klinik und Aetiologie der Hautatrophien, Arch. f. Dermat. u. Syph. **136**:198, 1921.

8. Volk, R., in discussion on Oppenheim: Arch. f. Dermat. u. Syph. **138**:336, 1922.

9. Brünauer, H. R.: Striae cutis distensae bei schwerer Shiga-Kruse Dysenterie, Ein Beitrag zur Pathogenese der Hautstriae, Arch. f. Dermat. u. Syph. **143**:617, 1923.

10. Kogoj, F.: Beitrag zur Aetiologie und Pathonogenese der Striae cutis distensae, Arch. f. Dermat. u. Syph. **149**:667, 1925.

dermatic and sclerodermatic changes combined with calcinosis and mucoid degeneration, which were also so clear in the case report recently published by Rottmann,[11] was emphasized by Jadassohn.[12] Telangiectasia is not seldom observed in scleroderma, and among others Becker[13] demonstrated that some so-called essential telangiectasia is based on hormonal disturbances.

Guillain, Alajouanine and Marquézy[14] as well as Besançon[15] mentioned the occurrence of juvenile cataract in persons with progressive scleroderma; Löwenstein[16] observed it combined with myxedematous changes, and Bowman and Clark[17] found it in a case of poikiloderma that showed histologic changes of the suprarenals.

We do not wish to enter into a discussion of the different publications concerning poikiloderma. As has already been stated, our cases cannot simply be classed under this name, although there is no doubt that certain relationships seem to exist. Lane has already summarized everything of importance that is known concerning this disease, and he came to the conclusion that "nothing is known of the etiology of poikiloderma"; Bowman and Clark[17] came to the same negative conclusion.

There are only a few more cases which must be especially mentioned in this connection. In his discussion of Lane's communication, Hazen[18] referred to a case of poikiloderma in which loss of sexual strength, headaches and adipositas occurred. Whitehouse[19] mentioned a combination of poikiloderma with hypothyroid and hypopituitary symptoms and hypogonadism; Müller[20] found the combination with exophthalmos and menstrual disturbances, and Cappelli[21] reported the occurrence of poikiloderma following partus.

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11. Rottmann, H. G.: Ueber Poikilodermia atrophicans vasculare (Jacobi) mit bemerkenswerten Nebenbefunden, Arch. f. Dermat. u. Syph. **153**:747, 1927.

12. Jadassohn, in discussion on Finger: Arch. f. Dermat. u. Syph. **119**:171, 1914.

13. Becker, S. W.: Generalized Telangiectasia, Arch. Dermat. & Syph. **14**: 387 (Oct.) 1926.

14. Guillain, G.; Alajouanine, T., and Marquézy, R.: Sclérodermie progressive avec cataracte double précoce chez un infantile, Bull. et mém. Soc. méd. d. hôp. de Paris **39**:1489, 1923.

15. Besançon, see Guillain, Alajouanine and Marquézy (footnote 14).

16. Löwenstein, A.: Hautveränderungen auf Grund von innern Sekretionsstörungen und Linsentrübung, Klin. Monatsbl. f. Augenh. **76**:539, 1926.

17. Bowman, K. M., and Clark, E. C.: A Case of Poikiloderma Atrophicans Vasculare, Arch. Dermat. & Syph. **15**:589 (May) 1927.

18. Hazen, H. H., in discussion on Lane (footnote 3).

19. Whitehouse: Poikiloderma, abstr., Arch. Dermat. & Syph. **10**:651 (Nov.) 1924.

20. Müller, R.: Atrophodermia erythematodes reticularis (Poikiloderm. atroph. vasc. Jacobi), Arch. f. Dermat. u. Syph. **109**:501, 1911.

21. Cappelli, I.: Poikilodermia atrophicans vasculare Jacobi, Gior. ital. d. mal. ven. **63**:617, 1922.

Certain other cases are, however, particularly interesting to us. They seem to show not only clear analogies to our cases but also that more or less poikiloderma-like changes are more frequently combined with endocrine disturbances than has previously been supposed. These cases are:

1. Bowman and Clark's case, which showed defective teeth, a cataract (not of the juvenile type) and a "distinctly feminine distribution of pubic hair," atrophy of the phalanges and a reduced basal metabolic rate. The autopsy in this case, however, failed to disclose distinct changes in the endocrine glands.

2. Even more closely related to ours is a case of Wertheim [22] in which the changes of the skin were strikingly similar to the ones we have described. Macroscopically and histologicaly, a marked atrophy of the hypophyses was found at autopsy. In this connection it must be mentioned that Wertheim as well as Hermstein described a case of striae cutis combined with acromegaly.

3. Leszczynsky's [23] case is also to be mentioned. Netlike and diffuse telangiectasia, atrophy and depigmented spots were combined in this case (whereas, hyperpigmentation was not observed). Besides these skin manifestations, a typical dystrophia adiposogenitalis and sexual impotence were present; roentgenologically, the sella turcica was found enlarged.

4. Since this paper was read, I have had occasion to observe another case which also falls into this group. It was presented by Prof. W. Lutz at the Swiss Dermatological Congress at Basle, in June, 1928.

It concerns a girl about 6 years of age, who presented on the skin the same changes that we have described, together with a double juvenile cataract, hypoplasia of the thyroid and a distinct pathologic endocrine habitus of the same type as that in our cases.

However, the connection of the different disturbances of the ectoderm (skin, hair, follicles, sweat glands, nails, teeth and lenses of both eyes) with marked changes of the endocrine system was not so evident in any previous observations as it was in our two cases. Since in our cases the sexual glands were undeveloped and functionally inadequate, and since the secondary sexual characteristics of the skin are directly dependent on the function of the sexual glands, it may be assumed with a high degree of probability that the changes of the skin

22. Wertheim, L.: Atrophie der Hypophysis cerebri bei einem der Poikilodermia atrophicans vasculare (Jacobi) nahestehenden Fall von Hautatrophie, Arch. f. Dermat. u. Syph. **150**:464, 1926.

23. Lesczynsky, R.: Zur Pathonogenese der Poikilodermia (Jacobi), Dermat. Wchnschr. **84**:321, 1927.

that we have described are in direct causal dependence on the anomaly of these glands. However, in consideration of the correlation of the various endocrine glands, one cannot exclude the possibility of a more complicated mechanism by way of other hormonal glands (above all, the pituitary gland and perhaps the thyroid). The dystrophia adiposogenitalis present in our second case, as well as in that of Leszczynsky, is in favor of this supposition.

CONCLUSION

If this communication is of value or interest, it lies in the fact that a pathologic condition of the skin has been demonstrated the causal connection of which with certain severe endocrine disturbances is beyond doubt. This has been done by simple observation of the facts without reference to theories and hypotheses. For the present, we must confine ourselves to such observations of facts and not to the setting up of wild hypotheses. In this way only can we make progress in the important problems of the relationship of pathologic dermatologic conditions to changes in the general organism.

LIPID STUDIES IN XANTHOMA*

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The relation of cholesterol to the cutaneous xanthomas apparently dates from the demonstration in the local lesions of crystals of cholesterol described in 1869 by Bazin,[1] and later corroborated by Mallassez [2] and Quinquaud.[3]

The demonstration by Chauffard and Laroche [4] and by others of a marked increase in the cholesterol content of the blood of patients having xanthomatous lesions has led to the view that the tumors in the skin and elsewhere are directly the result from one cause or another of a marked hypercholesterolemia.

The cause of this hypercholesterolemia has been variously ascribed to injury of the liver, pancreatic disease, diabetes and various other forms of constitutional diseases leading to disorders of fat metabolism.

If all cases of so-called xanthomatosis were uniformly associated with a coexistent or preexistent increase in cholesterol in the blood, the case for the cause and effect between the two might seem to be well proved.

However, here and there in the literature, one finds many cases of true xanthomatosis, in which careful blood analyses have failed to show an increase in blood cholesterol, and even an occasional case in which

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1. Bazin, quoted by Hillairet: Bull. Acad. de méd., Paris **7**:116, 1878; quoted by Carry: Ann. de dermat. et syph. **1**:64, 1880.

2. Mallassez, quoted by Laraiddy, E.: Thèse de Paris, 1877.

3. Quinquaud: Bull. de la soc. clin. de Paris **2**:259 (Nov. 28) 1878; Discussion of paper of Chambard, quoted by Siemens (footnote 7).

4. Chauffard and Laroche: Semaine méd. **30**:241, 1910.

this substance was found below the limits of normal. As early as 1921, Rosenthal and Braunisch,[5] in a carefully controlled case, failed to find a cholesterol increase in the blood, and stated their belief that hypercholesterolemia is not a necessary condition for the development of xanthomas.

They regarded the increase in the blood, as found by others, as more likely an important symptom accompanying the condition. Similar negative observations are recorded by Arzt,[6] Siemens[7] (one case), Herrmann and Nathan,[8] Greenbaum,[9] Turner, Davidson and White[10] (one case), Pulay[11] and by others.

If one analyzes many of the earlier reports, they are found to include a large number of cases of xanthoma palpebrarum, or xanthelasma. In the light of the present knowledge, these constitute a different disease entity, and do not properly come into the consideration of the true xanthomatous state.

Weidman,[12] after studying experimental xanthosis in man and in animals, concluded that perhaps cholesterol plays but an accessory rôle, and that other fatty substances may be the principal part in the production of the lesion. In this connection, Weidman was able to produce xanthosis in a dog, which never exhibited an increase in cholesterol in the blood.

A considerable degree of confusion regarding the rôle of cholesterol in the etiology of this condition, as well as its presence or absence in excess in the blood, are due to the various and more or less inaccurate methods for its determination.

The chemistry of lipid substances is still in a fluid state. Many of the earlier, as well as more recent determinations, have been carried on by spectroscopic and colorometric procedures, which are accepted as indicating gross changes, but are not as well adapted for quantitative determinations. Differences, as they exist in the literature, regarding the cholesterol content in the blood in xanthoma, to a certain extent, can be attributed to differences in methods of determination.

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5. Rosenthal and Braunisch: Ztschr. f. klin. Med. **92**:429, 1921.

6. Artz: Arch. f. Dermat. u. Syph. **126**:809, 1919.

7. Siemens: Arch. f. Dermat. u. Syph. **136**:159, 1921.

8. Herrmann and Nathan: Arch. f. Dermat. u. Syph. **152**:573, 1926.

9. Greenbaum, S. S.: Xanthoma with Erythema Telangiectodes and Parapsoriasis, Arch. Dermat. & Syph. **13**:291 (Feb.) 1926.

10. Turner, A. L.; Davidson, J., and White, A. C.: Edinburgh M. J. **32**:153, 1925.

11. Pulay: Dermat. Wchnschr. **73**:1036, 1921.

12. Weidman, F. D.: Studies in Hypercholesterolemia, Arch. Dermat. & Syph. **15**:659 (June) 1927.

In analyzing the cases in the literature in which marked cholesterol increases in the blood are recorded in the presence of the xanthomatic state, one is struck by the fact that many of these occur in diabetic patients, in a few in association with jaundice, and a large number in a group in which one is dealing with potential diabetic patients, e. g., cases of hyperglycemia and cases of low sugar tolerance. The occurrence of increased cholesterol content in the blood is an invariable accompaniment of pathologic lipemia (Bloor [13]). Lipemia is a frequent occurrence in such conditions as diabetes, tuberculosis, atherosclerosis, nephrosis (Epstein), and in many infectious diseases such as scarlet fever, typhus and pneumonia. The extremely high incidence of lipemia, with the associated increase in cholesterol in general diseases, and the extremely rare occurrence of xanthoma do not suggest an immediate cause or relationship between these two conditions.

Cholesterol being excreted in the bile, the most marked increases in blood cholesterol are found associated with jaundice. In those few cases in which jaundice and xanthomas have occurred, it must be self evident that additional factors must be present rather than the mere increase in the cholesterol content of the blood, in order to account for the absence of xanthomatous lesions in the vast majority of cases of jaundice.

In seeking for a cause for the production of xanthomatous lesions and the relation of cholesterol to such lesions, it would seem far more profitable to study cases in which the observations on the blood cholesterol were normal, since the same causes must operate in these cases as do operate in those in which a high cholesterol content is noted. It is held by some that the negative observations on the blood are not necessarily indicative of the fact that a hypercholesterolemia may not have at some time occurred. Most observers hold to the view that hypercholesterolemia is an essential forerunner to the production of cutaneous lesions.

During the past year, we have had the opportunity of studying three cases of xanthomas, all having existed under somewhat different conditions, and we believe that our investigations may throw a new light on the rôle played by the cholesterol. One of our cases was that of a patient with diabetes, in whom large numbers of xanthomatous lesions had existed for many years (fig. 1). The second case was that of an apparently healthy young man, in whom large numbers of xanthomatous lesions appeared abruptly, many as an exanthem, and have continued since (fig. 2). The third case was that of scattered xanthomatous lesions occurring in a young woman suffering from chronic arthritis (figs. 3 and 4).

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13. Bloor, W. R.: J. Biol. Chem. **49**:201, 1921.

REPORT OF CASES

CASE 1.—*History.*—B. B., a man, aged 42, came to the hospital because of an extensive eruption all over his body. The patient said that his father had diabetes mellitus, but was 71 years of age, and controlled his condition by diet. No other

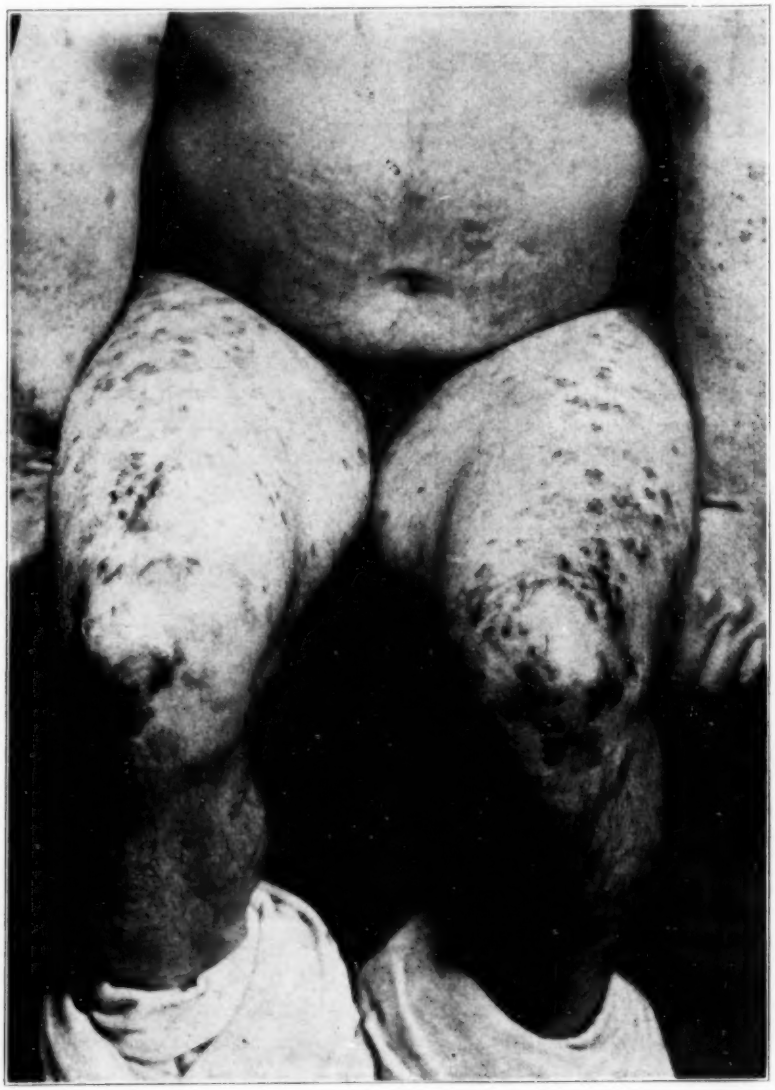

Fig. 1 (case 1).—Diabetes with extensive xanthomas.

member of the family had diabetes or any other chronic illness. The patient said that he had always enjoyed good health up to the time that the present eruption appeared. Five years before examination, an eruption in the form of yellowish papules and nodules, had appeared on the body. They first came over the region of the shoulders, extensor surfaces of the arms, and rapidly spread until they appeared

all over the body, with a special predilection for the buttocks, extensor surfaces of the arms and legs, and the hands. The patient had been obese for many years. When the eruption first appeared, he was seen by competent physicians, who told him that he had xanthomas, and who performed blood tests and urinalyses. He

Fig. 2 (case 2).—Young man with extensive xanthomas; nondiabetic.

was told that the urine did not contain sugar, and that the results of the analysis of the blood were normal. The lesions had persisted during all this time, and had given him considerable trouble, by reason of pain, particularly where they were subject to physiologic trauma.

Examination.—The patient was an obese man, who presented a large number of typical tuberous xanthomatous lesions all over the trunk, especially over the elbows, knees, buttocks and the backs of the hands. These varied in size from small, just visible, papules to groups of confluent lesions which were as large as a small pigeon's egg. The older lesions were extremely hard, and especially tender to pressure. The color of the lesions was a typical chamois yellow, and the disease had all the characteristics of a typical widespread xanthoma tuberosum. The mucous membranes were not involved. The remainder of the physical examination was negative. Biopsy of the small lesions showed early xanthomas, of the late lesions, the characteristic fibromatous change in association with these. On examination, the urine was found to be heavily loaded with sugar. The examination of the blood showed an enormous increase of circulating fats, which were demonstrated when the blood clotted by a serum which was creamy in appearance.

Diagnosis.—A diagnosis was made of xanthoma tuberosum; diabetes, and lipemia.

CASE 2.—*History.*—I. B., a man, aged 25, a student, had a family history that was negative. There was no history of diabetes or any other chronic disease in the family. The past history was negative, except for the usual diseases of childhood. The present illness began seven months before examination, with the sudden outbreak of an eruption over the chest and back. This eruption was not pruritic. It had persisted steadily, and gradually spread to the extremities. During this time, the patient felt well, had no symptoms suggestive of diabetes and had no loss of weight or other untoward symptoms.

Examination.—He was a somewhat obese young man, who presented an eruption, made up of discrete papules and nodules varying in size from that of a pinhead to that of a pea, over the entire body, including the face. These nodules had the characteristic saffron yellow color of xanthomas. They were firm to palpation, painless and did not show marked predilection for the elbows, knees or points of physiologic trauma. The mucous membranes were not involved. There was no jaundice, and the complete physical examination did not reveal any abnormality. There was no enlargement of the liver and spleen. The results of the urinalysis were negative, as were also the observations on the blood. The patient was advised to come into the hospital for prolonged observation and for chemical study.

Clinical Diagnosis.—A diagnosis was made of xanthoma tuberosum; this was substantiated by biopsy, which showed typical xanthomatous lesions, in which there were a large number of xanthoma cells, and a small amount of the fibromatous change which characterizes older lesions.

CASE 3.—*History.*—DeH., a woman, aged 19, referred from the department of medicine, had been under treatment for chronic arthritis involving most of the joints of her body. The arthritis had begun in the right elbow, and during the next four years involved all the joints of the extremities, except the shoulders. During the past month, she had been unable to walk. The joints were not red or swollen at any time. In her past history, her general health had always been good up to the onset of the arthritis six years previous to examination. She had no history of jaundice, polyuria, polydipsia or other symptoms suggestive of diabetes. In her family history there was nothing important bearing on her present illness. There was no history of diabetes or other chronic disease.

Examination.—The patient was a poorly developed and poorly nourished young girl. The most prominent observation consisted in definite fixation of the fingers in a position of flexure. There was a marked limitation of the left elbow joint, as

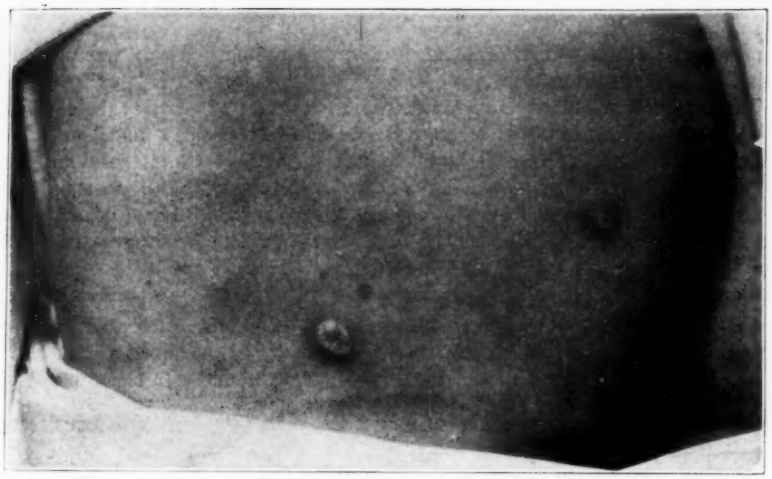

Fig. 3 (case 3).—Xanthomas occurring in patient with chronic arthritis (non-diabetic); lesions on the shoulders.

Fig. 4 (case 3).—Lesions on the buttocks.

well as in the wrist and fingers of the left hand. A considerable degree of limitation of motion in both knees existed without swelling. There was a marked limitation in the right ankle.

The cutaneous manifestations consisted in a number of discrete, bright yellow nodules, varying in size from a small pea to that of a bean, situated on the left shoulder, left buttocks, over the right knee and posterior aspects of both thighs and on the fingers of both hands. These had a characteristic chamois yellow color, and were surrounded by a bright erythematous halo. Some of the nodules had a distinct calcareous feel. The eruption was said to have appeared about a year and a half before examination over the legs, and had gradually spread to the back and shoulders. It had not given rise to any suggestive symptoms.

Clinical Diagnosis.—A diagnosis was made of xanthoma tuberosum; this was substantiated by biopsy, which showed characteristic xanthoma cells with marked fibrous hyperplasia, giving the characteristic picture of old xanthomatous lesions.

Biopsy had been done carefully in all three cases, and the microscopic pictures were shown to be typical of the condition, and identical in the three.

As these patients were all hospitalized, we felt that a new method of approach to the question was available in a careful chemical analysis of the tumors themselves. Numerous biopsies, therefore, were taken from all three cases, and these were analyzed as to their lipid content, by the most modern method available. The method employed was a modification of the Windaus digitonin procedure.

METHOD

Cholesterol was determined by the digitonin method described by Windaus, and the fatty substances were removed by the method of Kumagama Suto. Briefly stated, Windaus' method consists in adding digitonin to the alcoholic solution of the fatty substances. They were all saponified in the preliminary treatment of the tissue; the precipitated digitonids, therefore, represent all of the cholesterol—free and combined. The method of Kumagama Suto consists of first boiling the weighed tissue with a concentrated solution of potassium hydroxide. After cooling, the mixture is acidified; then extracted with ethyl ether. This removes all of the fatty substances as well as some impurities. The fraction is purified by first evaporating off the ether at a low temperature, and then extracting the residue with petroleum ether. In comparison with the other methods that have been suggested for cholesterol, the digitonin method is far superior.

Most of the other methods are colorimetric, and the presence of pigments occasionally gives erroneous results. Nevertheless, the colorimetric methods, particularly Bloor's and that of Myers and Wardell, will answer the question whether there are large amounts of cholesterol present in the blood, or what is usually considered normal amounts.

Before tabulating our results, we would like to direct attention to the determination of the cholesterol content of epithelium as determined by two of us (Eckstein and Wile) about a year ago (table 1). From table 1 it appears that cholesterol exists in the epithelium in the ratio of 20 per cent of the total lipids found. The analyses of the tumors

from the three cases are shown in the same table. It is evident that almost identical observations as to the fat content and cholesterol content were demonstrated in all three. The total lipids in the tumors, including cholesterol, are from 9 to 11 per cent by weight. Of the total lipids, cholesterol existed in all three cases to the extent of only 16 per

TABLE 1.—*Chemical Analysis of Xanthomas and Normal Cholesterol Values*

	Chemical Analysis of Tumors		
Patient	Total Lipids	Percentage of Cholesterol in Lipids	Percentage of Cholesterol in Tumor
DeH.	8.9	16.3	1.5
S.	11.7	17.0	2.0
B.	9.6	16.6	1.6

Normal Cholesterol Values in Man	
Of total lipids in blood	30%
Of total lipids in epithelium	20%
Of total lipids in subcutaneous fat	0.25%

TABLE 2.—*Influence of Fat Diet on Blood Lipids*

Patient DeH.	Total Lipids	Cholesterol
Fasting	401	148
2 hours after olive oil	401	152
4 hours after olive oil	478	147
6 hours after olive oil	461	148
Patient S.		
Fasting	439	110
2 hours after olive oil	467	115
4 hours after olive oil	600	111
6 hours after olive oil	508	119
Patient B.		
Fasting	2,300	316
2 hours after a meal	2,630	318
4 hours after a meal	2,769	302
6 hours after a meal	2,337	332

Cholesterol blood values	Mg. per 100 Cc.
Normal	120-180
Patient DeH.	169
Patient S.	110
Patient B.	403

cent. From this a striking fact is evident, namely, that although crystals of cholesterol may be found with great frequency in microscopic pictures of xanthomas, the bulk of the lipid material in such tumors are other fatty substances, cholesterol existing only to the extent of 1.5 per cent of the tumor by weight.

Our next investigations concerned themselves with the determination of cholesterol in the blood of the three cases under properly controlled conditions. Our results are shown in table 2. From these observations it is apparent that an enormous increase in circulating

fatty substances existed in our diabetic patient, and that normal values existed in the other two cases.

In our diabetic patient, two interesting and instructive experiments were performed. This patient had as high as 2,700 mg. of fat in his circulating blood per hundred cubic centimeters on a normal diet. This condition was coincident with a marked glycosuria.

When the patient was placed on a low caloric diet, in which fat was practically withdrawn, his tumors showed a marked recession, coincident with a loss in body fat. However, his circulating lipemia showed little change (table 3).

Later, the patient was placed on a diet directed toward the correction of his glycosuria. This diet contained a relatively large amount of

TABLE 3.—*Effect of Reduction Diets on Xanthomas*

Patient B. B., diabetic.

Diets						Urine Examinations on Diet			
Protein	Fat	Carbohydrate	Available Dextrose of Diet, Gm.	Calories of Diet	Days on Diet	Dextrose	Diacetic Acid	Effect on Tumors	Effect on Weight
50	50	200	234	1,450	21	(—)	(—)	Involution	Loss of 17 pounds (7.7 Kg.)
55	210	35	88	2,240	3	(—)	(—)	Involution	Total loss during this period 12 pounds (5.4 Kg.)
55	210	50	103	2,300	3	(—)	(—)	Involution	
55	210	100	153	2,500	3	(—)	(—)	Involution	
55	210	150	203	2,700	3	(—)	(—)	Involution almost complete	
55	210	175	228	2,800	3	(+++)	(++)	Involution almost complete	
55	210	300	353	3,310	30	(++++)	(++++)	Reappearance of tumors	Gain of 8 pounds (3.6 Kg.)
55	210	100	153	2,510	45	(—)	(—)	Almost complete involution	Neither loss nor gain

fat. Under these conditions, the tumors showed a more rapid disappearance. The fat content of the blood decreased more than half as he became sugar-free. The period of observation in this experiment was 111 days. From these facts, it would appear that our patient, under conditions of normal diet, established depots of fat in the skin. On a diet inadequate in calories, he withdrew fat from these depots to supply his required caloric needs. On a resumption of normal diet, these fat depots in the skin, xanthomas, reappeared (table 3).

When placed on a diabetic diet, at first below maintenance in calories but adequate in protein, the xanthomas again began to disappear. The diet now being raised by an increase in carbohydrates, he remained sugar-free, and the tumors continued to disappear even though he gained weight. This condition persisted even though the fat in his diet continued high. Tumor resolution and a decrease in lipemia occurred even when he was receiving five times the normal amount of dietary fat (figs. 5 and 6). This is entirely in accord with Bloor's

experiments in the relation of ingested fat to circulating fat in depancreatized dogs, and with that of Blatherwick,[14] confirmed by Marsh and Waller,[15] that there is no direct relation between the ingested fat in diabetes and the occasional lipemia which occurs as a complication of this condition.

Fig. 5.—Patient with diabetes, showing beginning involution of lesions under reduction diet.

To determine whether the two patients, whose blood was normal so far as fatty substances are concerned, belonged to the group of potential diabetes or to those with a low sugar tolerance, careful sugar tolerance

14. Blatherwick, N. R.: J. Biol. Chem. **49**:193, 1921.

15. Marsh, P. L., and Waller, H. G.: Relation Between Ingested Fat and Lipemia of Diabetes, Arch. Int. Med. **31**:63 (Jan.) 1923.

Fig. 6.—Complete involution in diabetic patient on reduction diet.

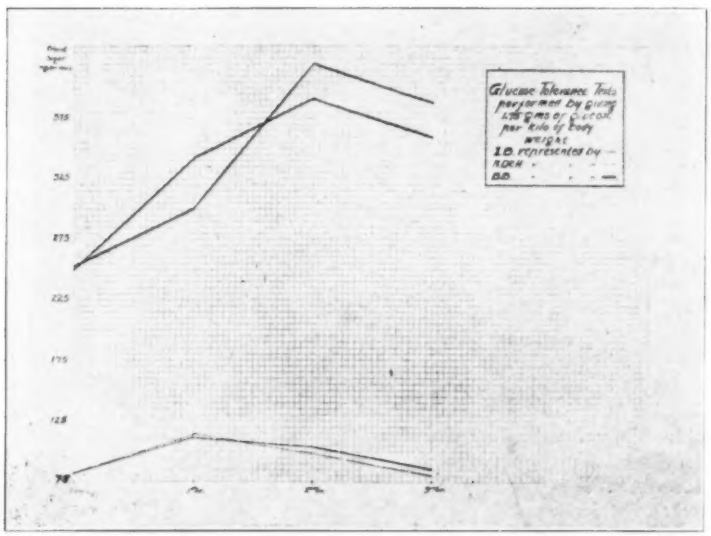

Fig. 7.—Chart, showing dextrose tolerance tests on the three patients.

tests were carried out on all three. Neither of the two patients showed the slightest lowered sugar tolerance, even when pushed to abnormal limits (fig. 7 and table 4).

The effect produced by the ingestion of large amounts of fat was carefully studied in all of the three cases. This experiment was carried out by giving the patients 100 cc. of olive oil after fasting. In none of the three cases was any unusual effect on the blood lipids noted (table 2).

Other features besides the increase in cholesterol in the blood have been suggested as operating not only for those cases of xanthoma in which the blood increase occurs, but also for those in which it is absent. Thus Rosenthal and Braunisch [5] suggested a local cellular change which shows an affinity for cholesterol, such functional change resulting from disturbances of the cholesterol output of the liver. Arzt [6] advanced

TABLE 4.—*Effect of Reduction Diets on Xanthomas*

Patient I. B., nondiabetic.

Diets			Available Dextrose of Diet, Gm.	Calories of Diet	Days on Diet	Urine Examinations on Diet		Effect on Tumors	Effect on Weight
Protein	Fat	Carbohydrate				Dextrose	Diacetic Acid		
50	50	200	234	1,450	21	(—)	(—)	Involution	Loss
55	210	35	88	2,240	3	(—)	(—)	Involution	Loss
55	210	50	103	2,300	3	(—)	(—)	Involution	No change
55	210	100	153	2,500	3	(—)	(—)	Involution	No change
55	210	150	203	2,700	3	(—)	(—)	No change	No change
55	210	200	253	2,900	3	(—)	(—)	No change	No change
55	210	250	303	3,110	3	(—)	(—)	Increase	No change
55	210	300	353	3,300	3	(—)	(—)	Increase	No change

the hypothesis that the xanthomatous condition is a systemic disease related, or partly related, to the recticulo-endothelial system. Herrmann and Nathan [8] stated that it is a constitutional change involving a pathologic ability of the involved tissues to pick up and store cholesterol. These are all hypotheses worth considering, but as yet not proved.

COMMENT

In three cases of typical xanthomas, by tissue analysis we have been able to demonstrate that identical cholesterol values in the local lesions exist for all three. We have further been able to show that the cholesterol is not increased in these tumors over the amount that is found in normal human epithelium. The largest part of the fatty content in the cutaneous lesions are lipids, other than cholesterol. In two of our three cases, the cholesterol values in the blood were normal in repeated examinations. In the third case, the cholesterol value in the blood was increased as part of a lipemia in association with the diabetic state. Here it should be noted that whereas the total fats were increased almost eight times the normal, the cholesterol was only increased twice

the normal. The xanthomatous lesions in our diabetic patient were markedly influenced by diet. An increase in sugar markedly increased the number of tumors. The withdrawal of carbohydrates from the diet, and a relative increase in ingested fat resulted in the recession and disappearance of many of the tumors. The increase in sugar and consequent caloric increase in the diet was followed by a marked increase in lipemia. A maintenance diet over six weeks caused a marked involution of all the lesions. It would appear that our diabetic patient established depots of fat in the skin coincident with lipemia, and withdrew fat from such depots when corrective dietary measures directed to the disturbed sugar metabolism were instituted.

Our remaining two patients did not show striking changes in their local lesions as the result of increased ingestion of sugar. In the young man with the exanthematous type of eruption, the tumors seemed to show marked retrogression when he was placed on a reduction diet. As he was somewhat obese, the disappearance of the fat from his tumors on a reduction diet might be explained on the consumption of his body fat consequent to the reduction diet. Both this patient and the one with arthritis were placed on diets which were high in fat, without a resulting increase in the number and size of the tumors.

That the production of xanthomatous lesions is probably due to disordered fat metabolism is presumptive. That cholesterol takes part in this disturbance as a component of body fats is also self evident. That an increased cholesterol in the blood is the primary cause of such tumors cannot be reconciled with the negative observation on the blood in our cases and in others, and in the chemical analysis of the tumors, which shows a cholesterol content not exceeding normal values for the epithelium, and far below the content of such lesions of other lipids.

Some other explanation for the production of these tumors must be sought than the supposition of hypercholesterolemia.

In this connection, some recent work by Smith[16] may have a special significance. Smith found that irritation and experimentally produced lesions in the region of the tuber cinereum in rats led to profound changes in fat metabolism. Animals thus traumatized developed an enormous increase in fat.

Hypothysectomized animals, on the other hand, developed emaciation and enormous increase in urinary output (diabetes insipidus). These experiments carry the suggestion that metabolic processes, notably the metabolism of fat, may be centrally located.

The marked disturbance of fat metabolism occurring in diabetes and in other diseases may possibly find its explanation in a central dis-

16. Smith, P. E.: The Disabilities Caused by Hyperphysectomy and Their Repair, J. A. M. A. **88**:158 (Jan. 15) 1927.

turbance as a result of the existing diseases. The suggestion that the distorted fat metabolism leading to xanthomatous lesions may also find its explanation in some central disturbance is also worth consideration.

CONCLUSIONS

1. The chemical analysis of xanthomatous lesions shows an excess of fatty substances other than cholesterol.

2. Cholesterol occurs in xanthomatous lesions to the extent of only 16 per cent of the entire lipids present, and only 2 per cent of the solid content of the lesion.

3. Xanthomatous lesions frequently occur with the absence of high values of cholesterol in the blood.

4. The lesions of xanthoma do not appear to be due primarily to cholesterol. This substance occurs in such lesions in a normal value with increasing amounts of other lipids.

5. The high cholesterol content of the blood in the lipemia of diabetes is an associated factor of the disordered fat metabolism, and not the primary cause of the xanthomatous lesion.

6. In the absence of diabetes, marked increases in alimentary fat do not appear to influence the formation or growth of xanthomatous lesions.

7. In diabetes, high alimentary fat per se does not affect the growth and development of the tumors, such growth and development being apparently dependent on the distorted fat metabolism associated with the diabetic state.

8. Apparently the best treatment for the xanthomatous state in the presence or absence of glycosuria would seem to be a reduction diet, treating such patients as one would obesity.

ABSTRACT OF DISCUSSION

DR. FREDERICK D. WEIDMAN, Philadelphia: I am in sympathy with Dr. Wile's deductions. I have always been struck, in the examination of frozen sections of xanthoma skin, with the preponderance of neutral fat in sudan III preparations. When the skin is examined by polarized light too, there is a comparatively small amount of cholesterol present in the tissues.

The general pathologist is aware of the frequency with which cholesterol develops in old fatty deposits like dermoid cysts. In the younger deposits there is likely to be a much lower proportion of cholesterol. I dare say the same considerations can be applied to these deposits as Dr. Wile encountered them. What is it we see in the younger most peripheral parts of the xanthoma lesions but the presence of neutral fats—the mobilization of normal fat? It is only in the older accumulations of fat in the center of the lesions that one is likely to pick up the lipoidal bodies.

I think it is likely that the disease is one of neutral fat metabolism, and that the appearance of cholesterol is due to a subsequent change in the molecular struc-

ture of the neutral fat. Perhaps the appearance of the cholesterol in the blood is due more to absorption from these fatty deposits in the skin and elsewhere than to the deposit of the cholesterol in the skin. All this is in harmony with the considerations outlined in connection with the deposit of fat in cysts, etc.

In reference to the xanthoma accumulations, perhaps there should now be demonstrated lipid tophi, instead of cholesterol tophi.

In regard to the ultimate basal metabolic processes, particularly those that have to do with associated hyperglycemia, I have been interested in experiments reported by Bickel, a Viennese, who stated that there may be depmetabolic forms related to diabetes but which are not expressed by the ordinary carbohydrates in the urine but by other carbonaceous materials. He tested this by comparing the total carbon of the urine with one of its more constant constituents, namely, nitrogen. This gives him a carbon-nitrogen ratio. Normally the ratio should be as 10:14; in disease it may be as 20:10—a high carbon ratio. That is one line along which I think we should proceed in attempting to explain these disturbances in xanthoma, some of which are associated with hyperglycemia and others of which are not.

PROFFESSOR BLOCH, Zurich: I had an opportunity to see these cases when I was in Ann Arbor, and to discuss them somewhat with Dr. Wile. I have not much to add to what I have already said to Dr. Wile, but I should like to emphasize the importance and interest of such investigations. They show again that the things which are going on in the living body are more complicated than we think, and in that I am a little disappointed by the results obtained by Dr. Wile. Until now the xanthoma was one of the few metabolic diseases of the skin in which we believed we could give a simple explanation. Our theory was that there was a pathologic metabolism of the cholesterol at the bottom of this disease, perhaps caused by a liver disturbance and followed by hypercholesteremia and that the deposit of cholesterins in the xanthomatous tissue was a simple consequence of the latter. Of course, we could not explain by this theory the particular localization of the xanthomas, for the term "cholesterinophilia," used by German authors for the localized affinity, does not explain anything. But the existence of a hypercholesteremia in the great majority of cases and the great amount of cholesterol in the tumors seemed to give us at least a certain basis for further investigations. Now we have to begin again, and that is why I am disappointed by Dr. Wile's communication. But facts are facts and we have to accept the truth, complicated as it may be. I think that Dr. Wile, who did this painstaking work, will agree that his researches should be continued with the same methods before we can undertake the building up of a new theory.

DR. SIGMUND POLLITZER, New York: Work of this kind is particularly important because we are in a state of great ignorance concerning the entire subject of the physiology and pathology of cholesterol. Cholesterol is a normal constituent of the tissues and is always present in the blood, as much so as sugar. The presence of a large amount of cholesterol does not necessarily result in cholesterol tumors, any more than the presence of a large amount of sugar means diabetes. Only in certain conditions, when there is a leakage of cholesterol into the tissues, do we find the development of xanthoma. Xanthoma once formed in the skin or other tissues is fairly permanent. It usually stays for a long period, until something happens that causes the absorption of the cholesterol deposit, which may almost entirely disappear, leaving only the reactive changes in the connective tissue. At any given time when the tumors have been formed, there may be no cholesterol excess in the blood; which proves one of two things, either there has been an excess in the past or the conditions which determine the leakage of cholesterol

through the capillaries, that necessarily precedes the formation of xanthoma, may be present in such degree that even normal amounts of cholesterol may make their way through the capillaries. We are completely ignorant of what these conditions are. For the localization that has been referred to, I think Dr. Wile and I offered a reasonable explanation, when we pointed out that the cholesterol tumors were in the vast majority of cases located where there are alternations of tension in the skin, at the elbows, knees, buttocks and around the joints, alternations of tension and pressure on the capillaries.

I think the paper demonstrated the fact that the formation of the tumors is not so simple as we thought years ago. It is not merely an excess of cholesterol in the blood that determines the tumor formation but this plus something else. We know nothing of the physiologic function and destiny of cholesterol. It is widely distributed throughout the animal and vegetable kingdoms and is present in most types of food. Every one eats a certain amount of cholesterol every day. What happens to it in the blood we do not know. That is a field for research which I hope will be taken up.

Dr. Udo J. Wile, Ann Arbor, Mich.: I realize fully that this contribution explodes, so to speak, preconceived ideas as to the nature of xanthoma. However, it is just another example of faulty deductions having been drawn from honest work in the past in which inadequate chemical methods were responsible for inaccurate results. The explanation offered by some that xanthomatous tumors are due to a peculiar affinity of a cell to attract cholesterol is no real explanation of the phenomena as they occur.

The fact that stands out from our contribution is that where the cholesterol content is highest in the blood under pathologic conditions one almost never finds xanthomatous lesions; that is, in pathologic lipemia and in jaundice.

The increase in cholesterol occasionally seen in a xanthomas always associated with diabetes is merely one phase of the disordered fat metabolism in the diabetic state.

There is some suggestive experimental evidence now at hand which may throw some light on fat metabolism and the deposition of fat in the skin. Evans and Smith have shown that if one removes the hypophysis from rats, they develop marked cachexia, and occasionally diabetes insipidus. If, however, they traumatized the base of the brain in the vicinity of the tuber cinereum, the animals developed enormous fat deposits all over the body. From this experiment, the suggestion is evident that the metabolism of fats may be centrally controlled.

The disordered fat metabolism accompanying certain pathologic states in the human being, may, therefore, be the effect of such pathologic changes on a central fat metabolic control.

We should like to reemphasize that according to our results, cholesterol plays a secondary rôle in the development of xanthomatous lesions. In the tumors themselves, it occurs in lesser values than it does in normal blood.

EXPERIMENTAL STUDIES IN ECZEMA

III. THE RÔLE OF THE SYMPATHETIC NERVOUS SYSTEM AND CALCIUM-POTASSIUM RATIO IN ALTERING CUTANEOUS IRRITABILITY IN THE RABBIT *

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AND
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PHILADELPHIA

REVIEW OF PRIOR STUDIES

In previous communications [1] studies were made of the calcium, magnesium, sodium and potassium content of the skin of rabbits under normal conditions, after various diets and after experimentally induced states. The cutaneous irritability of the same animals was first determined by noting the degree of reaction to external applications of dilutions of croton oil.

Correlating the degree of irritability and the mineral content of the skin, there appeared to be an inverse relation between the degree of irritability and the amount of calcium, and a direct relation between the degree of irritability and the amount of potassium. The less the irritability of the skin, the greater the likelihood of a high calcium content and a low potassium content; conversely, the more pronounced the irritability, the greater the likelihood of a low calcium content and a high potassium content. This relation was present in the majority, but not in all, of the animals studied.

The variation of the magnesium and sodium contents of the skin was so great that a correlation could not be made between such content and cutaneous irritability. A correlation could not be made between the degree of cutaneous irritability and the amount of total base. It was observed that such conditions that altered cutaneous irritability—diet, all green or oat diet; different experimental states—as nephritis or hepatitis, the injections of calcium or other chemicals—likewise altered the calcium-potassium ratio in the manner already stated.

The importance of calcium, magnesium, potassium and sodium metabolism to cellular activity; the antagonistic rôle of calcium and

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* From the Research Institute of Cutaneous Medicine.

1. Klauder, Joseph V., and Brown, Herman: Experimental Studies in Eczema I. Study of the Sensibility of the Skin of Rabbits to Chemical Irritants under Experimentally Induced Conditions, Arch. Dermat. & Syph. **11**:283 (March) 1925; Experimental Studies in Eczema II. A Correlation of the Chemistry with the Irritability of the Skin of Animals under Normal and under Experimentally Induced Conditions, Arch. Dermat. & Syph. **15**:1 (Jan.) 1927.

potassium in regulating cell function; the rôle that calcium plays in the phenomenon of inflammation and the effect of calcium in altering irritability of the cell were discussed and will not be reiterated.

In these prior communications, eczema was regarded as a pathologic process in which the cutaneous neurocellular mechanism is out of equilibrium. Biochemical changes which alter the neurocellular mechanism were discussed.

From the results of our studies and the review of the experimentation of others relative to the rôle that calcium, magnesium, sodium and potassium play in regulating cellular activity, it appears that the maintenance of this equilibrium is intimately concerned with the vegetative nervous system, and in relation to the latter, the endocrine glands, and can apparently be influenced through altered metabolism of divers origin.

Our conclusion that the irritability of the skin is in a large measure in relation to the calcium-potassium balance in the skin has recently been confirmed by Toyama and Hayashi,[2] who conducted a similar study.[3] They concluded that cutaneous sensibility to externally applied irritants does not always depend on the absolute amount of the single bases, calcium, magnesium, potassium and sodium, but that it can be more influenced by altering the relation of the single bases to one another. They state that the ratio of calcium and potassium is one of the most important factors in altering cutaneous sensibility, namely, marked decrease in sensibility is seen when the ratio is confined within the limits of 1:4 or 1:5.

CALCIUM-POTASSIUM RATIO AS AN AUTONOMOMIMETIC REGULATION

A peculiar relationship has been shown to exist between calcium and potassium salts. This has been demonstrated in the epochal work of Sidney Ringer[4] in his studies of the action of these salts on an isolated heart of a frog. As a result of Ringer's studies and subsequent

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2. Toyama, I., and Hayashi, H.: Studies on Lacquer Dermatitis V, Japanese J. Dermat. Urol. **26**:1091 (Dec.) 1926; Hayashi, H.: Experimentele Studien über die Empfindlichkeit der Haut gegen äussere Reize, ibid. **26**:721 (Aug.) 1926.

3. These investigators observed that variation beyond the limits in the ratio of calcium and potassium which acts in increasing the sensibility is likely to change the functions of the cells of the tissues by altering the hydrogen ion concentration of the skin. They were able to correlate cutaneous sensibility with hydrogen ion concentration of the skin, but not always with that of the blood when it is estimated electrometrically. In our studies we were unable to correlate the hydrogen ion concentration of the skin of rabbits with the irritability and with the calcium-potassium ratio in the skin.

4. Ringer, Sidney: Concerning the Influence Exerted by Each of the Constituents of the Blood on the Contraction of the Ventricle, J. Physiol. **3**: 380, 1880-1882; ibid. **4**:29 and 222, 1883.

work by others, notably Howell,[5] Zondek,[6] and Kraus and Zondek,[7] it has been shown that a proportion between the calcium potassium ion in the cells determines normal action in the heart by establishing an equilibrium between the action of the sympathetic and the vagus nerves. If the ratio of calcium to potassium is increased, a sympathetic action on the heart results, whereas if the ratio of potassium to calcium is increased, a vagus effect on the heart results. In the foregoing regard the action of sodium harmonizes with that of potassium. This principle is operative in the governing of other tissues—iris, vessels, bronchi, stomach, intestines, bladder and uterus, as shown by Höber.[8]

It further appears from the studies of Luithlen,[9] our own studies [1] and those of Toyama and Hayashi [2] that this principle is intimately concerned in governing the irritability of the skin.

PURPOSE OF EXPERIMENT

The calcium and potassium ratio in the skin is concerned in altering cutaneous irritability. This ratio plays an important rôle in establishing sympathetic and parasympathetic equilibrium. The foregoing as a scaffold for reasoning suggested experimentation in the direction of determining whether the obverse of this principle is operative, namely, that disturbance of the sympathetic or parasympathetic nervous system causes a disturbance of the calcium-potassium ratio, so that stimulation of the sympathetic (or depression of the parasympathetic) decreases irritability of the skin through augmentation of the calcium ion activity, and conversely, stimulation of the parasympathetic (or depression of sympathetic) increases irritability of the skin through augmentation of the potassium ion activity.

EXPERIMENTATION

For the purpose of our study, the only satisfactory means of disturbing the vegetative nervous system in rabbits was pharmacologically. The method of determining the irritability of the skin

5. Howell, W. H.: Vagus Inhibition of the Heart in Its Relation to the Inorganic Salts of the Blood, Am. J. Physiol. **15**:280, 1905-1906.

6. Zondek, S. G.: Untersuchungen über das Wesen der Vagus und Sympathikusreizung, Berl. klin. Wchnschr. **58**:1393, 1921; Deutsche med. Wchnschr. **47**:1520 and 1541 (Dec. 15) 1921; Das Ionengleich gewicht der Zellen, Biochem. Ztschr. **121**:86, 1921.

7. Kraus, F., and Zondek, S. G.: Kurze Vorläufige Mittelung über Verusche Betreffend die Rolle der Elektrolyte beim Herzschlag die Wirkung des Kochsolzes bei Verblutung und den Sogenannten Tonusstrom, Klin. Wchnschr. **1**: 996 (May 13) 1922.

8. Höber, R.: Physikalische Chemie der Zelle under der Gewebe, Leipzig, Wilhelm Engelmann, 1924, p. 689.

9. Luithlen, F.: Veränderungen des chemismus der Haut die verschiedener Ernährung und Vergiftungen, Arch. f. exper. Path. u. Pharmakol. **69**:365, 1912.

of rabbits was that employed in prior studies and described in detail in another communication.[10]

Briefly stated, a definite amount of croton oil diluted in olive oil was applied to the smooth skin; the inflammatory reaction was expressed in terms of from one plus to four plus reactions.

The following drugs were injected: atropine sulphate (complete paralysis of the peripheral distribution of the parasympathetic nerves); ephedrine (specific stimulation of the receptive mechanism of the entire sympathetic system); pilocarpine (stimulation of peripheral distribution of the parasympathetic nerves), and choline hydrochloride for its effect similar to that of pilocarpine.

Daily consecutive injections of these drugs were given intramuscularly. The following doses are per kilogram of weight. In most rabbits the total number varied from six to twenty-four. A few animals were given more injections (table 1). Atropine sulphate was injected in amounts varying from 0.002 to 0.010 Gm.;[11] ephedrine hydrochloride, in amounts varying from 0.001 to 0.010 Gm.;[12] pilocarpine hydrochloride mostly in amounts of 0.002 Gm.; choline was injected intravenously, 0.080 Gm. per kilogram of body weight; and histamine was injected intramuscularly in doses of 1 and 2 mg., and intravenously in doses of 0.5 mg. It was observed that the lethal dose intravenously was 1 mg.

Following the last injection, cutaneous irritability was tested and compared to that existing prior to treatment. The cutaneous irritability of the control rabbits remained essentially unchanged.

RESULTS OF EXPERIMENTS

Effect of Cutaneous Irritability.—It will be seen in table 1 that the irritability of the skin was decreased after injections of atropine in all of five rabbits treated. In four, the decrease was definite, whereas in one (12 K), it was slight. No correlation could be made in the degree of decreased irritability and the dosage employed. The irritability decreased in one rabbit (no. 81) after the injection of 0.002 Gm., in much the same degree as after the injection of 0.004 Gm. (nos. 82 and 85), and after ascending doses up to 0.010 Gm. (no. 108).

10. Klauder and Brown (footnote 1, first reference).

11. Tolerance to atropine is considerable in the rabbit and can be increased by habituation. (Sollman, A.: Manual of Pharmacology, ed. 3, p. 388). For this reason the dose was gradually increased in one experiment.

12. Dr. Carl Schmidt of the Department of Pharmacology, University of Pennsylvania, who extensively studied the pharmacologic action of ephedrine, informed us that the physiologic action of the drug in the rabbit is produced by the administration of 5 mg. per kilogram of body weight.

TABLE 1.—*The Effects on the Irritability and the Calcium Content of the Skin of Rabbits After the Administration of Autonomomimetic Drugs*

Rabbit No.	Compounds Injected	No. of Doses	Amount Injected Mg. per Kg. of Body Weight	Skin Irritability: Before Treatment, Dilutions of Croton Oil 1:5	1:10	1:20	1:30	1:50	Skin Irritability: After Treatment, Dilutions of Croton Oil 1:5	1:10	1:20	1:30	1:50	Skin Chemistry (Calcium): Before Treatment, Moisture, per Cent	Ash, Mg. per 100 Gm.	Ca, Mg. per 100 Gm.	After Treatment, Moisture, per Cent	Ash, Mg. per 100 Gm.	Ca, Mg. per 100 Gm.	Remarks
81	Atropine sulphate	8	2	3+	3+	2+	2+	+	2+	+	+	±	±	....	...	....	....	...	....	Marked decrease in skin irritability
82	Atropine sulphate	15	3	3+	3+	3+	2+	+	2+	+	+	±	±	....	...	....	....	...	. ..	Marked decrease in skin irritability
108	Atropine sulphate	21	up to 10	3+	3+	3+	2+	+	2+	+	+	±	±	....	...	....	....	...	....	Marked decrease in skin irritability
12 K	Atropine sulphate	22	5	3+	3+	2+	2+	+	3+	2+	2+	+	+	56.7	635	10.1	60.8	585	10.8	Slight decreased irritability; slight increased calcium content
85	Atropine sulphate	23	3	3+	3+	2+	+	+	+	+	±	±	±	....	...	...	....	...	....	Marked decreased irritability
1 T	Ephedrine.....	44	1	3+	3+	2+	+	±	2+	+	+	±	—	....	...	....	....	...	....	Marked decreased irritability
127	Ephedrine.....	47	1	3+	3+	3+	2+	+	3+	3+	2+	+	+	....	...	....	....	...	....	No change
4 P	Ephedrine.....	45	2	3+	3+	3+	2+	2+	3+	2+	+	+	±	....	...	....	....	. .	....	Marked decrease
1 K	Ephedrine.....	6	5	3+	3+	2+	2+	+	2+	+	+	—	—	....	...	....	....	...	....	Marked decrease
4 K	Ephedrine.....	13	10	3+	2+	+	±	±	+	±	—	—	—	58.3	783	8.9	62.5	833	14.9	Marked decrease; increased calcium content
210 C	Ephedrine.....	11	10	3+	3+	2+	+	—	3+	3+	2+	+	+	57.3	579	8.6	62.7	540	8.3	No change in skin irritability or calcium content
137	Pilocarpine.....	13	2	+	+	+	±	±	3+	2+	+	+	±	....	...	....	....	...	....	Marked increase
1 P	Pilocarpine.....	11	2	3+	2+	2+	+	+	3+	3+	2+	2+	+	....	...	....	....	. .	....	No change
15 B	Pilocarpine.....	6	2	2+	+	—	—	—	3+	2+	+	+	+	....	...	....	....	...	....	Moderate increase
5	Pilocarpine.....	11	2	+	±	—	—	—	+	+	—	—	—	....	...	....	....	...	....	No change
10 K	Pilocarpine.....	7	10	±	—	—	—	—	±	—	—	—	—	60.4	690	10.3	65.7	823	12.7	Unchanged irritability; increased calcium content
3 R	Pilocarpine.....	50	5	+	+	±	±	±	2+	+	+	+	—	62.7	757	13.5	65.5	698	12.9	Slight increased irritability; unchanged calcium content
80	Histamine.....	6	1	2+	2+	+	+	+	2+	+	+	+	+	....	...	....	....	...	....	Unchanged
79	Histamine.....	12	0.5	+	±	±	±	±	+	±	±	±	—	....	...	....	....	. .	. ..	Unchanged
6 B	Histamine.....	13	2	2+	+	±	—	—	2+	+	—	—	—	....	...	....	....	..	....	Unchanged
52	Choline.....	15	80	+	+	±	—	—	+	+	+	±	±	....	...	...	....	.	....	Marked salivation; unchanged
3 K	.....	..	..	2+	+	+	+	+	2+	+	+	+	+	59.6	805	12.1	63.1	765	14.1	Untreated control
9 K	.....	..	..	3+	2+	+	+	—	3+	2+	2+	+	—	62.8	631	9.5	60.6	775	10.1	Untreated control
1 J	.....	..	..	+	±	—	—	—	+	+	±	—	—	62.7	1,062	10.1	58.0	1,055	10.4	Untreated control
																	58.6	1,467	10.2	

The decrease in irritability following injections of atropine into rabbit 81 is pictorially represented. Figure 1 shows the pigmentation resulting, as is usual, at the sites of severe reactions following applications of the diluted croton oil and before treatment with atropine. Figure 2 shows the other side of the same rabbit, after treatment with

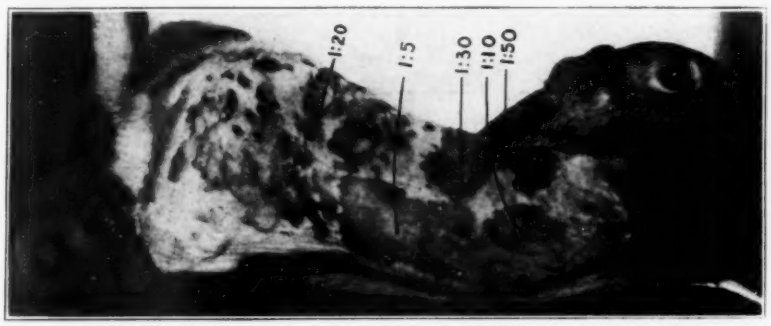

Fig. 1.—Right side of rabbit (no. 81) before injections of atropine sulphate, showing pigmentation appearing at all the sites of applications of different dilutions of croton oil, as marked in the photograph. The inflammatory reaction was severe, and as usual in such reactions, pigmentation appeared later.

Fig. 2.—Same rabbit as shown in figure 1, now showing the left side after injections with atropine sulphate and after applications of same dilutions of croton oil, as was employed in testing the right side, shown in figure 1. The reaction now was so less severe that pigmentation did not appear at any of the sites of application of the croton oil.

atropine. After the skin was tested in the same manner as in figure 1, the reaction was now much less severe, so that pigmentation did not appear.

Fig. 3.—Right side of rabbit (no. 1 +) before injections of ephedrine, showing considerable inflammatory reaction (superficial ulceration with edema and crusted surface) at site of application of 1:5 dilution of croton oil in olive oil. The remaining dilutions of croton oil applied, produced less of an inflammatory reaction without ulceration and are much less apparent in the photograph.

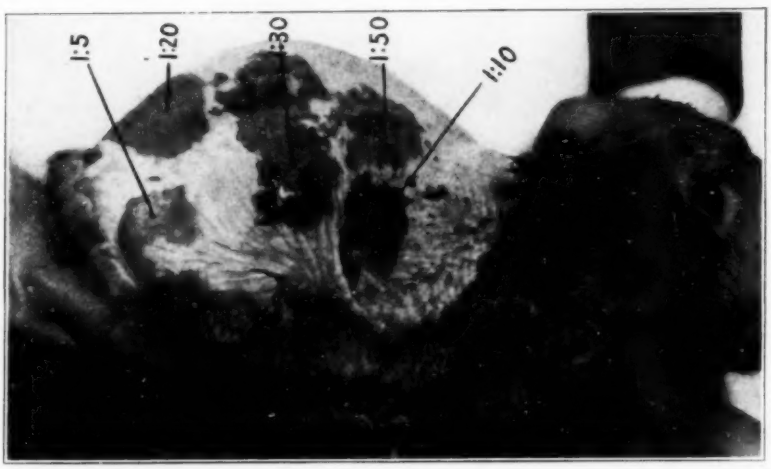

Fig. 4.—Same rabbit and same side as shown in figure 3, three weeks later (but before injections of ephedrine), showing pigmentation at all the sites of application of different dilutions of croton oil. The pigmentation shown usually appears on the skin of dark rabbits at the site of severe inflammatory reaction to externally applied irritants.

A decrease in cutaneous irritability was observed in four of six rabbits after injections with ephedrine. A striking decrease in cutaneous irritability was noted in one animal (4 K) after thirteen daily consecutive injections of 0.010 Gm., and in another animal (1 K) after six daily consecutive injections of 0.005 Gm. In the latter animal, two weeks after cessation of treatment, the skin was again tested; cutaneous irritability corresponded to that existing prior to treatment. A change in cutaneous irritability did not occur in the animal (127) given injections for a long period with 0.001 Gm., whereas a definite change occurred in another animal (1 T) similarly treated. In the latter animal the decreased cutaneous irritability is pictorially shown in figures 3, 4 and 5. In three of the six rabbits given injections of pilocarpine, the cutaneous irritability was increased.

Fig. 5.—Same rabbit as shown in figures 3 and 4, now showing the left side after injections of ephedrine and after application of the same dilutions of croton oil as applied to the right side. The inflammatory reaction now was so mild that the reaction shown in figure 3, or the pigmentation as shown in figure 4, did not appear.

A change in cutaneous irritability was not observed in the three animals given injections of histamine, nor in the one animal injected with choline.

It will therefore be seen from the results of the studies recorded in table 1 that the irritability of the skin of rabbits was altered by autonomomimetic drugs. The administration of such drugs did not uniformly alter cutaneous irritability, but it did so in the majority of animals.

Effect on Calcium-Potassium Ratio.—Five of the animals were killed at the end of the experimentation, and the entire skin was removed for chemical analysis for calcium, magnesium, potassium and sodium

TABLE 2.—*The Effect on the Irritability of the Skin of Rabbits After the Administration of Autonomomimetic Drugs and a Correlation of Altered Irritability with the Mineral Content of the Skin*

Rabbit No.	Compound Injected	Injection	Amount Injected Mg. per Kg. of Body Weight	No. of Doses	Skin Irritability: Before Treatment, Dilutions of Croton Oil 1:5	1:10	1:20	1:30	1:50	Skin Irritability: After Treatment, Dilutions of Croton Oil 1:5	1:10	1:20	1:30	1:50	Mineral Content of Skin After Treatment, Mg. per 100 Gm. Dry Skin: Ca	K	Mg	Na
81	Atropine sulphate	Intramuscularly	2	8	3+	3+	2+	2+	+	2+	+	+	±	±				
82	Atropine sulphate	Intramuscularly	2	9	3+	3+	3+	2+	2+	+	+	+	±	±				
			4	6	...	...	...	...	...	2+	+	+	±	±	66.6	107	41	267
108	Atropine sulphate	Intramuscularly	2	1	3+	3+	3+	2+										
			3	1														
			4	8														
			6	1														
			7	1														
			8	1	...	...	...	. .	...	2+	+	+	±	±				
			9	2	...	...	...	...	...	2+	+	+	±	±				
			10	9	...	...	...	...	...	...	...	...	...	...	51	172	38	257
1 T	Ephedrine.....	Intramuscularly	1	44	3+	3+	2+	+	±	2+	+	+	±	—	40	345	33	333
85	Atropine sulphate	Intramuscularly	2	15	3+	3+	2+	+	+	3+	2+	+	+	±				
			4	8	...	...	...	...	...	+	+	±	±	±	54	272	38	305
137	Pilocarpine.....	Intramuscularly	2	13	+	+	+	±	±	3+	2+	+	+	±	42	364	32	344
1 P	Pilocarpine.....	Intramuscularly	2	11	3+	2+	2+	+	+	3+	3+	2+	2+	+				
127	Ephedrine.....	Intramuscularly	1	47	3	3+	3+	2+	+	3+	3+	2+	+	+				
4 P	Ephedrine.....	Intramuscularly	2	45	3+	3+	3+	2+	2+	3+	2+	+	+	±				

(table 2). In three animals (82, 108, 137) the amount of calcium and potassium correlated the altered irritability of the skin following the administration of the drugs employed. As already mentioned, in a previous study, we correlated the calcium and potassium content of the skin with its irritability. In one of the two remaining animals (85) the amount of calcium correlated the altered irritability, but the amount of potassium did not. In the remaining animal (1 T) the calcium and potassium content did not correlate the altered irritability. It was not possible to determine the mineral content of the skin before the study, and again at the end of the study, but it would appear from these studies, that in four of five animals, the calcium-potassium ratio was altered by the administration of autonomomimetic drugs.

Before the completion of these studies, however, we found it possible to remove from the rabbit a piece of skin sufficiently large for the determination of calcium alone, without disturbing the health of the rabbit, and a similar piece at the end of the study. The result of this study is listed in table 1.

Determinations of calcium were made in the foregoing manner in five rabbits. In the rabbit (12 K) treated with atropine there was a slight decrease in cutaneous irritability and a slight increase (0.7 mg.) in the calcium content. Although this slight increase was within the experimental error, which is about 1 mg., it was in the expected direction. Two of the rabbits were treated with ephedrine. In one (4 K) a marked decrease in cutaneous irritability occurred with a marked increase in calcium (6 mg.). These were the most striking results in the series. In the other animal (210 C) there was no change in the cutaneous irritability or in the calcium content. One (10 K) of the two remaining rabbits treated with pilocarpine did not show any change in cutaneous irritability but an increase of 2.4 mg. in calcium occurred; in the other (3 R) there was a slight increase in irritability with a slight decrease (0.6 mg.) in calcium. Again, this decrease was within the experimental error, yet in the expected direction.

It will therefore be seen that in four of the five rabbits studied, the calcium content of the skin correlated the cutaneous irritability, whereas in one (10 K) a discrepancy occurred.

Control Studies of Calcium.—Three rabbits were employed as controls. Two weeks after testing the cutaneous irritability, a second piece of skin was removed for determination of calcium, and cutaneous irritability was again tested. In one of the rabbits, a third piece of skin was removed two weeks after the second piece. In this rabbit (1J), the three determinations of calcium yielded results within 0.3 mg. In this one, as in the remaining animals, cutaneous irritability remained

unchanged. In the other rabbit (9 K), the second determination of calcium was 0.6 mg. more than the first. In the remaining rabbit (3 K), however, the variation was 2 mg.

COMMENT

The basis of our experimentation—the obverse of the principle that calcium and potassium ratio determines sympathetic and parasympathetic equilibrium—is logical when subjected to the laws of thought. When pragmatically considered in relation to the skin, it is necessary to bear in mind that the only cutaneous structure that is definitely known to be innervated by the parasympathetic nervous system is the sweat glands. Pertinent to our studies is the comprehensive experimentation of Luithlen and Molitor [9] who demonstrated that intracutaneous injections increased the irritability of the sympathetic as well as the parasympathetic nervous systems as manifested by their response to pharmacologic irritation. Moreover, the obverse of the foregoing principle seems not unreasonable in view of the pharmacologic experimentation in the direction of showing the influence of nervous control of biochemical processes.

If the mechanism controlling carbohydrate mobilization is under nervous control, it would seem possible that its activity might be modified reflexly. In a study of the action of autonomomimetic drugs and of vagal stimulation on the output of sugar and of fluid from the hepatic veins of the terrapin, Snyder, Wells and Culley [13] showed that epinephrine produced an increase in the output of sugar and volume outflow, whereas, pilocarpine elicited a decrease in the output of sugar and fluid. Stimulation of the peripheral ends of the vagi caused a diminished output of fluid and of sugar.

It was demonstrated by Griffith [14] that stimulation of the central ends of the crural, sciatic or vagus nerve in cats and rabbits causes a prompt increase in the blood-sugar level, even after the suprarenals have been removed, the nerves to the liver, pancreas and hypophysis cut and the thyroid parathyroid apparatus completely removed.

Britton [15] has shown that stimulation of the right vagus nerve in cats produces hypoglycemia as long as the stimulation is maintained.

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13. Snyder, C. D.; Wells, H. S., and Culley, P. G.: Autonomic Control of Liver Function, 1. The Action of Autonomomimetic Drugs and of Vagal Stimulation upon Fluid and Sugar Output from the Hepatic Veins of the Terrapin, Am. J. Physiol. **66**:485, 1923.

14. Griffith, F. R., Jr.: Reflex Hyperglycemia; The Carbohydrate Mobilization Effected by Afferent Crural, Sciatic and Vagus Stimulation, Am. J. Physiol. **66**:618, 1923.

15. Britton, D. W.: Studies on Conditions of Activity in Endocrine Glands; Nervous Control of Insulin Secretion, Am. J. Physiol. **74**:291, 1925.

He demonstrated that the action is specifically caused by the effect of this stimulation on the pancreas. The output of epinephrine may be increased by stimulating the sympathetic nerve supply of the suprarenal glands, directly or through a dorsal center. This may increase the rate of the discharge of epinephrine to about four times the normal (Stewart and Rogoff [16]). Moreover, Billigheimer, Dresel and Katz [17] observed that stimulation of the sympathetic nerve through the administration of epinephrine lowered the calcium content of the blood. They expressed the opinion that calcium is deflected from the tissues and is increased in the cells of the organs innervated by the sympathetic nervous system.

After reviewing pharmacologic experimentation relative to the rôle that the calcium-potassium ratio plays in establishing sympathetic and parasympathetic equilibrium, Pulay [18] emphasized the importance of this principle in relation to the altered cutaneous irritability in eczema.

In further discussing results herein reported, it is important to bear in mind the rôle played by the arteriole and capillary system in the phenomena of inflammation. In inflammation, the circulatory phenomena are conspicuous and are regarded by a large school of pathologists as the primary and essential symptoms. Krogh [19] concluded from his studies that dilatation of capillaries involving mechanical stretching of the endothelium cannot take place without being accompanied by an increase in the permeability, an increase which runs on the whole, parallel to the degree of dilatation.

The vascular actions of the autonomomimetic drugs employed in this study could not be correlated with the altered cutaneous irritability which these drugs produced. For example, according to Krogh,[19] epinephrine does not cause capillary constriction in the rabbit, although it does in man and in the cat. Although we employed ephedrine in our study, it has been shown that this drug has the same pharmacologic action as epinephrine. Moreover, atropine, which causes a cutaneous vasodilatation, decreased the cutaneous irritability. Again, choline which causes an intense vasodilatation of the skin, did not alter cutaneous irritability, nor did histamine, which causes relaxation of the arterioles. This action of the drug in the rabbit has been demonstrated by Lewis.[20]

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16. Stewart, G. N., and Rogoff, J. M.: The Spontaneous Liberation of Epinephrin from the Adrenals, J. Pharmacol. & Exper. Therap. **8**:479, 1916.

17. Billigheimer, Dresel and Katz, quoted from Pulay: Ekzem und Urtikaria, Berlin, Urban & Schwarzenberg, 1925, p. 52.

18. Pulay, E.: Ekzem und Urticaria, Berlin, Urban & Schwarzenberg, 1925, p. 56.

19. Krogh, A.: The Anatomy and Physiology of Capillaries, New Haven, Yale University Press, 1924, p. 237.

20. Lewis, Thomas: The Blood Vessels of the Human Skin and Their Responses, London, Shaw & Sons, 1927, p. 109.

CONCLUSION

Cutaneous irritability in the rabbit was altered following the administration of autonomomimetic drugs. It was decreased following the administration of atropine sulphate and of ephedrine hydrochloride and decreased after the injection of pilocarpine hydrochloride. Cutaneous irritability was changed in most, but not all of the animals treated. The change was striking in some animals.

A change in cutaneous irritability did not occur after the administration of drugs that produce a cutaneous vasodilatation, namely, choline and histamine.

It would appear from data submitted that the calcium-potassium ratio in the skin of four of five rabbits was altered by the administration of autonomomimetic drugs.

Determinations of the calcium of a piece of skin of the same rabbit, before and after the administration of autonomomimetic drugs, changed in four of five rabbits in the direction of correlating the changed cutaneous irritability.

It would appear from evidence herein submitted that the autonomic nervous system is concerned in altering cutaneous irritability in the rabbit, perhaps through a disturbance of the calcium-potassium ratio.

SUMMARY

Prior studies of conditions which alter cutaneous irritability in the rabbit are reviewed. There appears to be an inverse relation between the degree of cutaneous irritability in the rabbit and the calcium content of the skin and a direct relation between the degree of cutaneous irritability and the potassium content of the skin. Experimental data are reviewed which show that the calcium-potassium ratio acts as an autonomomimetic regulator.

Experimentation was planned to study the obverse of this principle when applied to the skin. The vegetative nervous system in rabbits was pharmacologically disturbed. The following drugs were injected intramuscularly daily for from six to twenty-four consecutive injections: atropine sulphate, ephedrine hydrochloride, pilocarpine hydrochloride, choline hydrochloride and histamine.

Cutaneous irritability was tested prior to treatment and at the end of treatment. Some rabbits were killed at this time, and the skin was analyzed for calcium and potassium content which was correlated with the change in cutaneous irritability. In other rabbits, a piece of skin was removed for the determination of calcium only, and a second piece at the end of treatment for similar analysis.

As a result of these experiments it was concluded that cutaneous irritability in the rabbit was altered following the administration of autonomomimetic drugs, and was decreased following the administration of atropine sulphate and of ephedrine hydrochloride. Cutaneous irritability was changed in most, but not in all, of the animals treated. The change was striking in some animals.

A change in the cutaneous irritability did not occur after the administration of drugs that produce a cutaneous vasodilatation, namely, choline and histamine.

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The obverse of the principle that ion-ratio of calcium and potassium determines sympathetic and parasympathetic equilibrium is discussed in relation to other pharmacologic experimentation in the direction of showing the influence of nervous control of biochemical processes and also in relation to the results of the study herein reported.

THE OCCURRENCE OF TUBERCULOID REACTIONS IN THE INGUINAL GLANDS IN EARLY SYPHILIS*

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WITH THE TECHNICAL COLLABORATION OF EDWIN KERSTEN, M.D.
MINNEAPOLIS

The inguinal glands in early syphilis have been carefully studied by almost all of the older syphilologists. In more recent times, Zurhelle [1] made a detailed histologic investigation of the inguinal glands in early syphilis and reported extensively on his observations.

The purpose of the following study was to examine the inguinal nodes in early syphilis and to determine the frequency of the occurrence of tuberculoid structure.

MATERIAL

Inguinal nodes were excised from twenty-nine persons with early untreated syphilis. In all of the cases the diagnosis was clear and beyond doubt.

The excised nodes were bisected. One half of the gland was utilized for routine staining, while the remainder was treated by Levaditi's method for demonstrating spirochetes.

Frequency of Occurrence of Tuberculoid Structure in Twenty-Nine Cases

	Syphilis I Wassermann Reaction Negative	Syphilis I Wassermann Reaction Positive	Syphilis II Wassermann Reaction Positive
Number of cases	5	9	15
Banal reaction	4	8	9
Tuberculoid reaction	1	1	6

Total cases: 29
Banal reaction: 21
Tuberculoid reaction: 8

It will be noted from the accompanying table that in eight of the nodes tuberculoid structure was found. What is the significance of this

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1. Zurhelle, Emil: Histopathologische Studien an syphilitischer Lymphdrüsen des primären und sekundären Stadiume, Dermat. Ztschr. **34**:1 (Aug.) 1921; Zur Histopathologie der rezent syphilitischen Lymphdrüsenkrankung, Deutsche med. Wchnschr. **38**:**1**, 1921; Der Histopathologie der rezent syphilitischen Lymphdrüsenkrankung, Arch. f. Dermat. u. Syph. **38**:366 (April 15) 1922.

observation? In order to answer this question we must briefly define our views concerning the provocation of tuberculoid reaction.

For the modern view of specific tissue reactions we are indebted to Lewandowsky, Kryle, Bloch and others who have carefully observed the variations in the histologic response of the same person when subjected to the action of a specific organism under different conditions. The writings of these authors have been freely consulted in the preparation of this communication.

The histology of the syphilitic chancre, macule or papule is comparatively unvarying. The tuberculoid structure is entirely lacking in a chancre except in a lesion which has been allowed to remain untreated for several months. In macules and papules, with the exception of the miliary lichen syphiliticus, tuberculoid reactions are not found. Only after the disease has existed for approximately two years do excised lesions show tuberculoid structure with any degree of consistency.

The age of the infection and the tissues involved must influence the type of inflammation which can occur when areas react to the presence of spirochetes. If a person who has never had syphilis is infected with the disease, and he reacts in the usual manner, in the course of three weeks a lesion is found at the site of inoculation which is clinically and histologically a chancre. Chancres may vary in size, contour and gross appearance, but they are essentially identical microscopically. In and about the chancre certain substances must be formed, which are absorbed into the lymph and blood streams. These substances, when they come in contact with the tissue cells, prepare them to react against the invading spirochetes in a manner different from that in which the tissues reacted at the site where first infection took place. If a person with a chancre is reinoculated with living spirochetes, he does not develop another chancre. The lesion which is formed at this new site of inoculation is a papule. Microscopic examination of this papule reveals a chronic proliferative and exudative type of inflammation. If, however, a person who is harboring a latent or old syphilitic infection is inoculated with living spirochetes the resulting lesion is a gumma, and the microscopic examination reveals tuberculoid structure.

Why in the course of eight weeks after a syphilitic infection does the body respond with an eruption of macules or papules instead of with the development of numerous chancres? Why do the lesions become less numerous the older the infection and why does the type of inflammation change from banal to tuberculoid?

This faculty of the tissues to react differently at different times in the stage of a disease may be explained on the grounds of a change of allergy. For every stage of syphilis, whether it is primary, secondary,

tertiary or latent, there apparently is a corresponding state of allergy, and the response of the tissues to invading spirochetes at these various stages produces a definite corresponding clinical and histologic lesion.

In tertiary syphilis the state of allergy must be extremely high, as there is a maximal reaction to an exceedingly small number of organisms, for they can be revealed only after a prolonged search.

The clinical and anatomic late syphilitic lesion is a gumma, and the ability of tissues to respond with gummous formation is an enduring one, as is evidenced by the appearance of tertiary lesions years after the primary infection. Tabetic persons and persons having certain other forms of cerebrospinal syphilis may develop gummas of the skin, but in the paretic person this power is lost; an important histologic fact established by Kyrle. The histology of a gumma is that of a so-called specific granuloma; here tuberculoid structure is constantly found.

Enlargement of the inguinal nodes and later the occurrence of a generalized adenopathy in a fresh syphilitic infection is an established fact. Adenitis in syphilis may be looked on as a defense mechanism. We would be more inclined to view this as a localized reaction against the spirochetes rather than to think of the nodes serving as barriers against generalization. If one reviews the anatomy of the lymphatic system and realizes the tremendous drainage area from a small focus, one is impressed with the fact that the enlarged inguinal nodes accompanying a chancre on the penis are only a part of the lymphatic tissue involved, and that the older the infection the greater the amount of adenoid tissue which is brought into participation against the invaders. In our studies we found tuberculoid structure occurring in the inguinal nodes in approximately one fourth of the number examined. If we accept the view that tuberculoid structure is brought about because of a high degree of tissue response, then if tuberculoid reaction occurs in the lymph nodes long before it does in other lesions, which may be studied by biopsy, it seems to us that we are correct in asserting that a high grade defense is set up in the lymphatic system early in the course of syphilis. In our examinations, therefore, we were concerned largely with determining the frequency of the occurrence of tuberculoid reactions in the inguinal nodes in early cases of untreated syphilis.

PRIMARY SYPHILIS

In our series there were six persons with chancres and a negative Wassermann reaction of the serum. In five of this number the histology of the inguinal nodes revealed a nonspecific, subacute lymphadenitis, while the node excised from the sixth person showed undoubted tuberculoid structure.

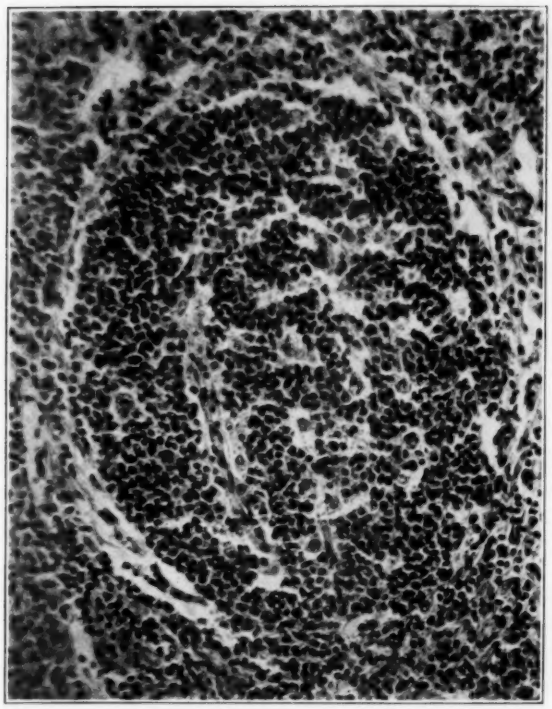

Fig. 1.—Banal, nonspecific, subacute inflammation in an inguinal node in early syphilis.

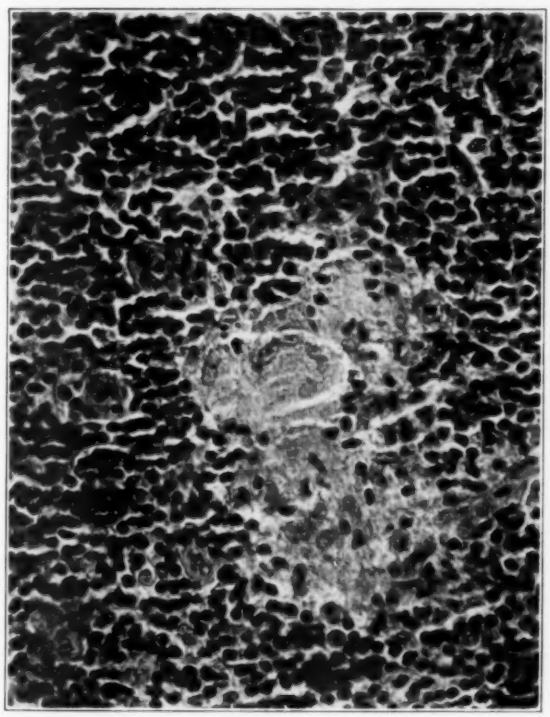

Fig. 2.—Beginning tuberculoid reaction in an inguinal node in primary lesion.

In our series of primary syphilis, the remaining nine persons had positive Wassermann reactions of the serum. Of these, eight nodes were grouped under the classification of nonspecific banal inflammation, while one node revealed typical tuberculoid structure. In summarizing the observations on the nodes excised from fourteen persons with only chancres, we may report that twelve nodes showed nonspecific banal inflammation and two nodes revealed tuberculoid structure.

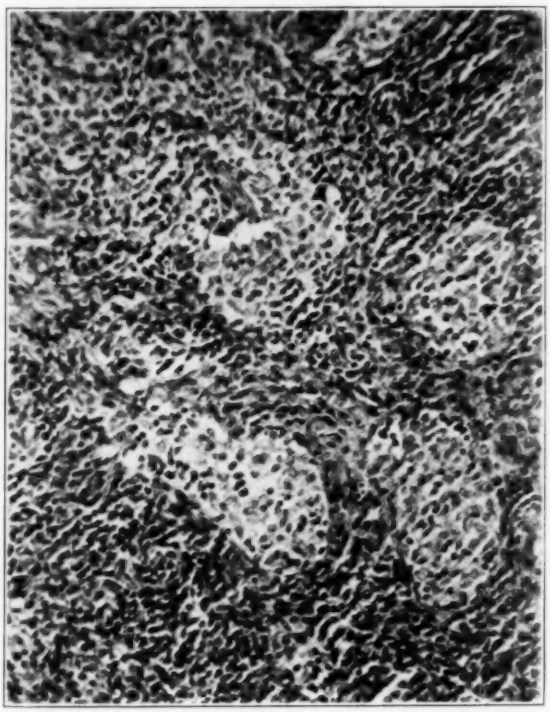

Fig. 3.—Epitheloid or indurative tuberculoid structure, occurring in an inguinal node in early secondary syphilis.

SECONDARY SYPHILIS

We examined the inguinal nodes excised from fifteen persons who presented generalized early syphilitic eruptions and positive Wassermann reactions of the serum. Nine specimens of this number were classified as showing nonspecific banal inflammation, while six nodes revealed such marked tuberculoid structure that when we submitted the preparations to our pathologic staff, they unhesitatingly stated that, in the light of their previous knowledge, the sections showed all of the requirements for a diagnosis of tuberculosis.

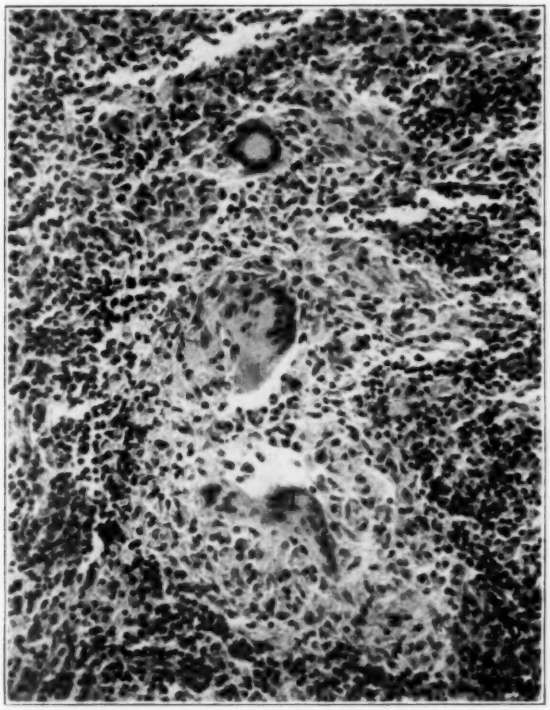

Fig. 4.—Typical tuberculoid structure, occurring in an inguinal node in early secondary syphilis.

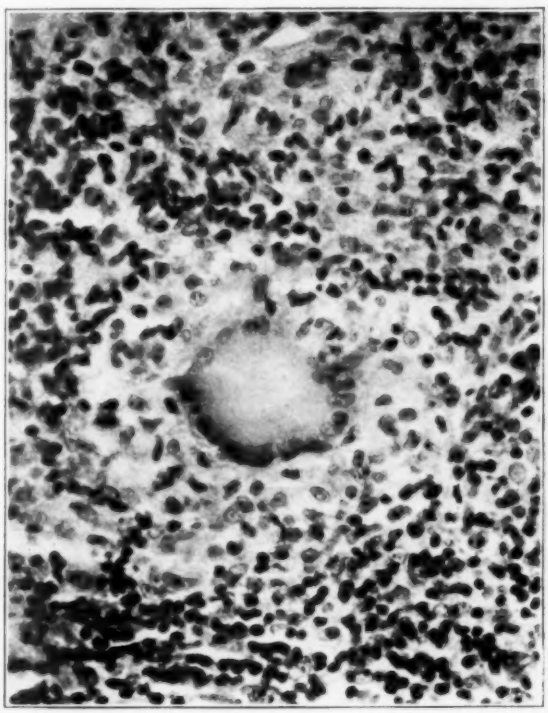

Fig. 5.—Detail of "tubercle" found in an inguinal node in early secondary syphilis.

COMMENT

None of the standard textbooks on pathology nor any of the literature that we have been able to find mentions the occurrence of tuberculoid structure in the inguinal nodes in early syphilis. Finsterlin [2] described an example of softening of an inguinal gland in early syphilis, but microscopically tuberculoid tissue was not found. Zurhelle evidently did not find tuberculoid reactions in his studies. This is probably due to the fact that in his series he examined only five nodes from patients with secondary syphilis. It will be noted in our table that there were nine nodes from patients with secondary syphilis which showed only banal inflammation, and had these cases constituted our entire series, we, too, would not have discovered tuberculoid structure.

There was no essential difference noted in the primary and secondary nodes which showed only banal inflammation. The observations when these preparations were used were not uniform. Some sections showed many cells which when stained with Pappenheim's solution could be interpreted as plasma cells. From one patient we excised a large papule as well as a node for the purpose of comparison. In the papule we found an unusually large number of plasma cells, while in the section of the gland there were practically none. In none of the sections of nodes did we find collections of plasma cells which were to be compared to the number present in an area of infiltrate of equal size, occurring in a cutaneous papule.

In certain sections we found marked thickening of the walls of the arteries at the hilum. New capillaries, too, were frequently encountered. Lymph follicles varied greatly in number. In some of the nodes they were distinct; in others they could not be distinguished.

Here and there we found small collections of polymorphonuclear leukocytes, but we could not state that in the particular case there had not been a mixed infection.

Eight of the total number of twenty-nine nodes examined showed the presence of tuberculoid reaction. One of these nodes was excised from a patient with a chancre and a negative Wassermann reaction of the serum; one from a man with primary syphilis in whom the Wassermann reaction was positive, and the remaining six were excised from patients with early secondary syphilis.

Two distinct types of tuberculoid tissue were found. In the first the adenoid tissue was almost entirely replaced by closely packed epitheloid cells, compressed into lobules, which were separated by thin strands of lymphoid cells. The sections resembled preparations made from advanced lesions of sarcoid of Boeck. This type of so-called epitheloid or indurative tuberculoid structure involved almost the entire node.

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2. Finsterlin, A.: Ueber die Histopathologie der Drüsenweichung in Frühstadium der Lues, Dermat. Wchnschr. **70**:97 (Feb. 14) 1920.

The second type of tuberculoid reaction noted might be likened to that found in miliary tuberculosis. In these sections, the striking observation was the occurrence of small collections of epitheloid cells containing one or several giant cells. These "tubercles" were found scattered throughout the adenoid tissue or in adjacent areas, especially in the vicinity of the hilum. Occasionally, several small foci of tuberculoid structure appeared to have coalesced, making a rather extensive area, which had every appearance of an area one might encounter in tuberculous adenitis, with the exception of the fact that there was no caseation. In none of the nodes was necrosis found, but in certain localities the cells stained poorly and appeared pale. In five of the eight nodes showing tuberculoid structure we found spirochetes in the sections stained by the Levaditi method.

SUMMARY

It is hazardous to conjecture on the significance of the presence of tuberculoid structure in the nodes excised from eight persons freshly infected with syphilis. Suffice it to state, that the histology of the inguinal nodes in early syphilis is variable and that two distinct types of pathologic changes are encountered. One is a subacute proliferative and exudative inflammation which may be termed nonspecific lymphadenitis; the other is a tuberculoid reaction which histologically is indistinguishable from that found in tuberculous adenitis.

If the tuberculoid reaction is characteristic for a high degree of allergy, and it appears to be, then from a comparison of the histology of the chancre, the macule or the papule with the accompanying inguinal enlargements, we may infer that tuberculoid structure is found much earlier in the lymphatic lesions than in cutaneous lesions or lesions of the mucous membranes. As general adenitis and the positive Wassermann reaction occur at approximately the same time in the course of syphilis, possibly this early tuberculoid reaction has a decided bearing on the formation of antibodies.

CONCLUSIONS

1. The inguinal nodes from twenty-nine persons with early untreated syphilis were excised and examined microscopically.

2. Banal nonspecific inflammation occurred in twenty-one specimens.

3. Tuberculoid reactions were observed in eight nodes.

4. Tuberculoid structure was found much earlier in the inguinal nodes in early syphilis than in cutaneous lesions.

5. If the tuberculoid reaction is a manifestation of high resistance, then probably the production of immunity or antibodies begins early in the lymphatic system.

ABSTRACT OF DISCUSSION

DR. JOHN H. STOKES, Philadelphia: I should like to have an opportunity to commend this work of Dr. Michelson's as an initial step in a more modern study of the pathologic physiology of syphilis. What is particularly needed at the present time is a study of the mechanism of the interaction between the *Spirochaeta pallida* and tissue cells, rather than the mere examination of the histologic appearances. It may well be possible to imitate the methods recently adopted for the study of tuberculosis and to apply a technic of microdissection to the study of such a series of tissues as Dr. Michelson presents. This might make it possible to bring the organism of the disease into direct contact with certain types of isolated cells, in order that the entire action might be studied. It is to be hoped that Dr. Michelson will feel encouraged to continue his investigations in these newer fields.

DR. UDO J. WILE, Ann Arbor, Mich.: I wish to express my appreciation of this demonstration, and to ask Dr. Michelson whether he attempted any staining to show to what extent in these lesions, in which the tubercle-like reaction took place, this reaction corresponded to herds or masses of spirochetes. One possible explanation of such a reaction might be in the nature of a reaction of a foreign body, the giant cells playing a phagocytic rôle.

DR. LLOYD W. KETRON, Baltimore: Apropos of Dr. Wile's remarks, I have been doing some work on the type of reaction of the tissues of animals to the acne bacillus. After the intradermal injection of this organism a granuloma is produced, frequently associated later with the formation of giant cells. In these giant cells I have not been able to demonstrate the bacillus of acne, although innumerable ones are demonstrable in the early stages of reaction. Apparently, the organism is destroyed or converted into a nonrecognizable substance. This may be the case with the spirochete.

PROFESSOR BLOCH, Zurich: Not only is this work of interest as a study in the pathologic anatomy and in the histologic changes of syphilis but it is far more interesting from a general standpoint, because it is a new contribution to an important and general rule. Formerly, twenty or thirty years ago, pathologists believed that such a tubercular structure was specific for a tuberculous infection; now we know that this structure can be found in many diseases. It was discovered long ago in leprosy by Jadassohn, then in tertiary syphilis, in sporotrichosis, etc., and we find it in trichophytosis and in the blastomycosis of the European type. It is a rule, which is important for general pathology, that whenever this structure is present the disease has reached its allergic stage. It is not specific for the infection by Koch's bacilli, therefore, but typical for a certain form of the reaction of the allergic organism in many other infectious diseases. This can be seen clearly in trichophytosis. The superficial trichophytosis has not this structure, but in the trichophytic granuloma of the Kerion one finds histologic changes which could be taken for typical tuberculosis. Even if trichophytin is injected intradermally into patients who are allergic, one can find the same structure that is found on the injection of tuberculin into tuberculous patients. I think that these changes are histologic expressions of the biologic fact of allergy, and Dr. Michelson's investigations would be of even much more far-reaching importance if he had at the same time followed the course of the allergic reactions not only by the Wassermann test but by the use of luetin.

The rule that tuberculous structures are found not only in tuberculosis but in many other infections, when allergic conditions are present, is not sufficiently known and considered by pathologists. They much too often make the diagnosis of tuberculosis on seeing these structures. Herein lies the practical importance of these observations.

It has been stated by Jadassohn that when in leprosy the tuberculous structure is present the bacilli are extremely rare; that is a general rule also. Therefore, I should rather expect that if Dr. Michelson will search for spirochetes in such glands, he will not find them, or at any rate, rarely.

DR. CHARLES J. WHITE, Boston: I agree with Professor Bloch's theory of the giant cell rather than Dr. Wile's. Dr. Wile says that it is due to herds or masses of bacilli, but in lupus vulgaris one has to average ninety sections before a single organism is found.

DR. WALTER J. HIGHMAN, New York: May I add my encomiums to those already expressed to Dr. Michelson concerning the material in his paper and the stimulating manner in which it was presented. I should also like to emphasize its brevity.

I think that Professor Bloch has analyzed very well for us the significance of the tuberculous unit in so many conditions, in contradistinction to the older view which obtained that this particular picture was regarded as typical of tuberculosis. Nevertheless, the significance of Dr. Michelson's paper is so great that I hope if he is sufficiently ingenious he will manage to rule out other conditions which could cause a similar picture, notably tuberculosis itself. I do not believe that this could be accepted as expressing tuberculosis of the glands that are in regional relation to the primary lesions; nevertheless, there is such a possibility, particularly since the tubercle bacillus is specific. I hope that in spite of all the obvious difficulties, those depending on the recognition of the various organisms in this condition and the known viability of the organism if they are present, and other handicaps, he will be able to prove that these glands are syphilitic in every instance. In that way he will lead up to a solution of many of the questions Professor Bloch mentioned.

DR. JAMES HERBERT MITCHELL, Chicago: About five years ago Dr. Ormsby and I saw a case of primary syphilis of the inner canthus of the eye in which the glands had been removed surgically on that side. In all, the patient had had about six hours of operative work under ether. The pathologist reported that the glands were tuberculous. The surgeon thought the process was probably not tuberculous but was unable to say what it was.

In connection with the presence of spirochetes in the glands in cases of secondary syphilis, you are all familiar with the ease by which spirochetes can be aspirated from the glands and demonstrated by means of the dark-field examination.

DR. ERWIN P. ZEISLER, Chicago: Many of the excisions of the inguinal glands were done on patients in our service at the Cook County Hospital, and the diagnosis of early syphilis was verified before they were sent to Dr. Michelson. The excision apparently had no unfavorable effect on the course of the disease, and healing took place by primary union in all cases.

DR. HAROLD N. COLE, Cleveland: The question comes up as to whether any relation exists between the amount of change here and the number of spirochetes which are present. We all know that the inguinal gland is the first gland to become swollen after the infection of syphilis. We can all remember the time when it was customary to advise the excision of the primary point of infection, thinking thereby to get rid of a large part of the syphilitic infection in that way. We know now that the spirochetes spread rapidly. This has been shown by Brown and Pearce, Kolle and others. By rubbing in a preparation of spirochetes on an abraded surface, the inguinal gland is infected promptly, and spirochetes have been found within five minutes in glands 5 cm. away from the abraded surface. Other glands do not respond with the promptness that the regional gland shows, possibly

because not so many organisms come in contact with them, but in time they show the same histologic picture.

I wish to express my appreciation of this piece of work which was so well presented.

DR. MICHELSON, Minneapolis: I wish to thank the gentlemen for their kind discussion of my paper. I am not familiar with the type of work which Dr. Stokes refers to, but I am sure there is much room for experimentation along the line of tissue cultures.

In regard to finding the spirochetes, we stained one half of each gland, side by side, with a piece of positive syphilitic liver, using the Levaditi method. When we did not find spirochetes easily, we usually were successful on continued search. As is known, it is harder to distinguish cells by this method; so we could not definitely state the precise position of the spirochetes. Professor Bloch clearly stated his position concerning specific tissue reactions, and since he is a pioneer in this work, I can only emphasize his statement, that the general pathologists have been slow to ascribe other etiologic factors than tubercle bacilli to the formation of tuberculoid structure.

Dr. Mitchell brought out an important point, that inguinal glands are rarely excised in acute conditions for diagnostic purposes.

I do not believe that there need be a tuberculous terrain for the formation of the tuberculoid structure; I think that this is dependent on the allergy of the patient. Answering Dr. White's question about the age of infection, we found tuberculoid structure more frequently after the twelfth week of infection.

Professor Pinkus, of Berlin, in his excellent monographs on syphilis, has always emphasized the fact that the size of the glandular enlargement did not correspond with the severity of the infection, nor was the adenopathy diagnostic. We did not find a connection between the size of the gland and the tuberculoid reaction.

DERMATITIS VEGETANS

REPORT OF TWO CASES OF THE HALLOPEAU TYPE*

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As vegetation occurs in many dissimilar dermatoses, in both the benign and the malignant type, the subject of dermatitis vegetans presents a most complex problem. In cases that occur secondarily to some well recognized dermatosis, for example, as in cases of eczema reported by Wende, Pusey, Hartzell and others, the dermatologist's responsibility in differentiation is not so great as in cases of the continued or recurring types, in which grave constitutional conditions must be considered. In 1889, Hallopeau described a benign type of continued recurring dermatitis with vegetations. His article caused considerable controversy, never satisfactorily concluded, regarding the relation of this dermatitis to accepted malignant conditions; even though cases of this type have been reported from time to time, the problem of their acceptance as a clinical entity remains unsolved.

A group of five cases were presented in which Hallopeau described a classic primary lesion at the onset of the eruption, and also showed a distinctive difference from other vegetating dermatoses in the mode of progression by peripheral extension. He maintained his views regarding the condition as an entity for a number of years, during which confliction as to the classification of similar vegetating dermatoses developed; he finally concluded that his type of eruption rather favored that in Neumann's cases of pemphigus vegetans, rather than the others, and in writing a book with Leredde he included the condition under the title "maladie de Neumann," which included pemphigus vegetant de Neumann, dermatite pustuleuse chronique en foyers a progression excentrique et pyodermite vegetante d'Hallopeau, dermatite herpetiforme vegetante de Brocq, Hudelo et Wickham, erytheme bulleux vegetant d'Unna and condylomatose pemphigoide maligne de Tomasoli.

In an attempt to correlate these various cases, two main types were recognized, the bullous and the pustular, and it was claimed that the two forms, generally independent of each other, could develop successively in the same person. This was considered a strong factor in distinguishing the condition from common pemphigus vegetans as well as from dermatitis herpetiformis vegetans. This view, however, was not substantiated, as one finds in the description of symptoms that the

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primary lesions consisted of either bullae or vesicopustules and that the two were rarely observed in the same case. The disease was considered curable, the suppurating form being considered more benign than the exclusively bullous type. This resulted from a comparison of the cases of Hallopeau and of Neumann. Deaths occurred in two of five cases observed by Hallopeau and in one death was ascribed to an intercurrent erysipelas; this was in striking contrast to eight or nine deaths reported by Neumann, the total number of cases observed by him not being stated. In a differential diagnosis, the disease was not to be confused with pemphigus vulgaris vegetans, dermatitis herpetiformis vegetans or impetigo herpetiformis. It was claimed that the condition as described under the name "maladie de Neumann" constituted a special and distinct disease in spite of the denials of Kaposi, Köbner and Herxheimer, who considered it a form of pemphigus vulgaris.

The dermatitis was considered due to a local infectious agent, which multiplied in the integument and developed foci by autoinoculation in successive localizations. Thus, while Hallopeau has been accredited by writers as describing "dermatite végétante" as a variety of pemphigus, he did not include it in the fatal variety that is known today, and there is no evidence to show that he ever considered it other than a benign condition.

In Hallopeau's description, the main features of initial onset were given as raised circular patches of pustules the size of millet seeds on inflamed indurated bases surrounded by erythematous areolae. The lesions enlarged by peripheral extension as the patch dried in the center and developed crusting; removal of the crust exposed a pigmented papillary base. These lesions frequently advanced and coalesced to involve large areas in exuding pustular lesions. The main sites of predilection consisted of the genital region, lips, mouth, fingers, neck and back.

REPORT OF CASES

The cases here reported agreed with Hallopeau's description, and corresponded in morphologic detail with each other.

CASE 1.—*History.*—J. M., a man, aged 47, born in the United States, single, a repairer of automobiles, had an eruption on the skin. His father died at the age of 60, from an unknown cause. His mother died at the age of 28 of "heart disease." Two brothers died in infancy. In childhood, he had had measles and diphtheria and eighteen years before admission he had had gonorrhea. His general health had always been good; there was no history of any skin eruption preceding the present condition, which had begun about three years before admission, when he had noticed a single "hard pimple" on the inner side of the right thigh from which he had squeezed a "white fluid." Gradually new lesions had appeared, forming circular patches which dried as they advanced from the border and developed elevations.

Examination.—When the patient came under observation at the Newark City Hospital, the eruption had involved the groins and had spread out over the thighs and lower part of the abdomen and backward over the perineum through the crural fold, over the buttocks and downward on the thighs. Upward, the eruption involved the back to the midlumbar region, spreading out like a fan. Other locations became affected, including the scalp, face, arms and feet. The scalp was almost completely involved with an exuding pustular dermatitis. The mouth remained free. Lesions were never observed on the buccal mucous membrane. A lesion located at the corner of the mouth advanced over the surface of the lip but did not extend into the mucous membrane of the mouth.

Fig. 1 (case 1).—Active spreading lesions. The right groin shows the dry keratotic character of the lesions as pustulation subsided.

New lesions were always inclined to be circular in outline and consisted of slightly raised, closely grouped flat pustules the size of a pinhead, with a peculiar deep bluish-red or violaceous, erythematous, rather hard base. The lesions, which had vesicopustular borders, progressed slowly, as they dried in the center and became somewhat flattened and deeply pigmented, clinically resembling epidermophytosis. Gradually the keratotic vegetations developed, projecting in irregular papillomatous masses, and deep sulci followed the natural lines of cleavage. These masses were elevated from one-fourth to one-half inch (0.6 to 1.2 cm.) or more, and a foul-smelling, mucopurulent discharge exuded from the depressions. The only subjective symptom was a painful sensation in locations of skin apposition, especially in the region of the scrotum and thighs.

Physical examination gave negative results. The temperature, pulse and respiration remained normal. Laboratory examination, including the Wassermann reaction and urinalysis, gave negative results. Blood taken from the lobe of the ear showed an eosinophilia of 10 per cent, and blood taken from the erythematous area around a lesion showed this condition increased to 25 per cent. There was also a moderate lymphocytosis; otherwise, nothing unusual was noted. X-ray examination of the chest and gastro-intestinal tract gave negative results. Examination of the mouth showed three teeth with apical abscesses.

Fig. 2 (case 1).—Irregular papillomatous masses with deep sulci following the natural lines of cleavage.

Histologic Examination (Dr. Highman).—Under low power magnification, the section was seen to consist of a highly altered epidermis and massive infiltration. The epidermis was thickened, the pegs proliferating widely. They branched in all directions, in places uniting to snare off papillae. This formed islands in which there was an infiltration as well as the main infiltration in the body of the corium.

Under high power magnification, the minute histologic changes in the epidermis appeared not to be of any particular significance. Those usually found in hyperplasia were present. A great many wandering cells were present.

The composition of the infiltration was manifold. Lymphocytes, plasma cells, epithelioid cells and a few eosinophils were found, in no particularly ordered

arrangement. Clusters of pus cells were seen, especially in the snared off papillae. The capillaries were all dilated, and distinct general edema was present in the corium. The larger vessels had inflamed walls and swollen endothelium.

The picture was that of a vegetating granuloma. It did not resemble any of the specific infections, but might well be pyogenically altered or engendered granulation tissue. For this reason, the section must be interpreted as showing dermatitis or pemphigus vegetans.

Tissue and cultures were sent to the Pathological Laboratories, University of Pittsburgh.

Fig. 3 (case 1).—Eruption spreading over perineum through crural fold, out over buttocks, downward on the thighs and upward to the midlumbar region.

Report by Dr. Andrew Wallhauser: A growth of *Aspergillus, Staphylococcus* and a *Micrococcus* was obtained. *Aspergillus* grew on special prune Sabouraud's agar, and showed the following morphologic characteristics: spores from 4.6 to 5 microns in diameter, globoid and faint yellow; no ascospores; hyphae from 4.5 to 7 and from 5 to 14 microns in diameter; occasional branching, smooth, some septate; foot organ present; conidiophore, globoid, blackened or greenish; sterigmas, one simple unbranched, spores in short chains. These observations are characteristic of *Aspergillus repens.*

A rabbit was inoculated in the ear, and developed a hard brownish-pink induration that lasted about ten days. Further experiments in inoculation with this organism will be reported later.

The staphylococcus was identified as *Staphylococcus epidermidis* of Welsh. The micrococcus consisted of a slowly growing gram-positive coccus arranged in masses. The colonies were small and discrete, white and moist. Cultural reactions showed that dextrose, lactose, sucrose, mannite, salicin, inulin, raffinose or litmus milk were not fermented. Gelatin was not liquefied and showed a fine white surface growth.

The organism was not a member of the staphylococcus or streptococcus groups, and is classified as a micrococcus on the basis of morphology and cultural characteristics. Animal inoculations showed it to be mildly pathogenic.

The patient in case 2 developed only *Staphylococcus epidermidis*—Welsh.

Treatment.—All teeth were extracted on account of the presence of a decided pyorrhea in addition to the infection of the teeth shown in the x-ray examination. Injections of arsphenamine, antimony and potassium tartrate and a bismuth preparation were tried without apparent benefit. After various local antiseptic remedies were employed with only moderate improvement, the vegetating masses were removed down to the skin level, a curet being used under local anesthesia. There was considerable hemorrhage, which was readily controlled with firm compression. Wet dressings of mercuric chloride were applied, and the patient was given daily baths of sodium borate alternated with mercuric chloride 1:4,000. Under this plan, slow but steady and uninterrupted improvement resulted.

The patient was discharged from the hospital in June, 1927, all lesions having disappeared except a small area in a state of regression at the corner of the mouth. Five months later, he was again admitted; the lesion present when he was discharged was increasing in size, and two lesions in the scalp had recurred. All other locations were free from eruption and presented a healthy aspect, but still showed the presence of the peculiar violaceous pigmentation, with a moderate parchment-like crinkling and punctate scarring. He afterward had several mild recurrences, which were readily controlled with antiseptic treatment.

Case 2.—The patient was shown before the New York Dermatological Society with the following history, which is here included through the courtesy of Dr. Howard Fox.

W. C. S., a man, aged 39, born in the United States, of German gentile ancestry, was a retail grocer. His parents were living and well. His family history was unimportant. With the exception of measles in childhood, he had always enjoyed robust health previous to his present illness. About four years before, he had suffered from a severe sore throat and had been treated with diphtheria antitoxin; he had recovered in two weeks. Six months later, tonsillectomy and hemorrhoidectomy had been performed. About one month later, his mouth had become very sore with what he called "canker sores." After that he had had recurring attacks of sore mouth. Coincident with the beginning of the oral lesions, the meatus had become red and covered with "blisters." These had persisted until the time of presentation. About six months after the appearance of the blisters on the meatus, "blisters" had appeared in the left groin; these had become confluent and had spread.

From June 10 to Sept. 1, 1927, the patient had been under observation at the Johns Hopkins Hospital. According to a copy of the hospital records in the patient's possession, definite diagnosis of the lesions in the mouth or on the meatus had not been made. Those in the genitocrural region had been treated as granuloma inguinale with antimony and potassium tartrate without benefit. A

total of 62 cc. of 1 per cent solution in divided doses (the number not being stated) had been given. A diagnosis of "papillomatous venereal wart" was then made from a histologic examination. The lesions had been treated by "fulguration and had practically disappeared at time of discharge." The lesions in the mouth were not benefited by treatment. A smear showed a few Vincent's organisms, and one opinion was expressed that both the mouth and the meatal lesions were caused by Vincent's angina. Arsphenamine was suggested but not used, though previous to coming to the hospital the patient had received one intravenous injection of arsphenamine without any benefit.

The patient also presented a pustular condition of one great toe, which had appeared shortly before his admission. This was considered to be due to an ingrowing toenail. While he was in the hospital the great toe of the opposite foot became similarly affected. Treatment by ultraviolet light was given the meatal lesions, and a meatotomy followed by the passage of sounds was performed with only slight benefit. Only negative evidence was obtained from the various laboratory tests. A blood count showed the red and white cells to be within normal limits. A differential count showed a marked eosinophilia. The Wassermann test was negative. The urine did not show abnormal ingredients, and the blood sugar showed 85 mg. to 100 cc. of blood.

Dental examination "ruled out the teeth as a factor" in his disease. Cultures from lesions in the groin showed colon bacilli, from the toe, *Staphylococcus albus* and from the mouth the "usual mixed growth of normal mouth organisms." The temperature had been afebrile, except on one occasion when an intravenous injection of mercurochrome-220 soluble had been followed by a sharp reaction.

The patient first came under Dr. Fox's observation eleven days previous to his presentation, at which time several of the lesions gave a different picture from that of the present. There was practically nothing abnormal in the mouth at that time. The lesions in the genitocrural region were decidedly more elevated and papillomatous, though later they flattened considerably under x-ray treatment. The feet also presented a vesiculosquamous appearance suggestive of eczematoid ringworm. At the time of presentation, there was a profuse vesiculobullous eruption of the greater part of the mouth, including the hard and soft palate and lips. On the meatus was a bright red, superficially, ulcerated smooth lesion about a third of an inch (0.8 cm.) in diameter. In the genitocrural and anal regions were a number of papillomatous and partly ulcerating lesions from which there was a seropurulent discharge of bad odor. They varied in size from that of a pea to 1½ inches (3.7 cm.) in the longest dimension. There was also an irregular area of scar tissue, the size of a palm, the result of former treatment. The toes and part of the tarsus of the left foot were swollen, painful and tender and were covered by numerous discrete and coalescing pustules suggesting the picture of a dermatitis repens. Cultures were made from the papillomatous lesions, but growth had not appeared at the time of presentation. Cultures from the foot showed *Staphylococcus aureus* and from the mouth a pure streptococcus. The urine was normal, except for a marked amount of indican. Tissue from one of the papillomatous lesions in the groin did not show Donovan bodies or blastomyces. Histologic examination by Dr. Highman showed a granuloma (infections, probably due to fungus). The patient was of dark complexion, was tall and athletic looking and weighed 170 pounds (77.1 Kg.). He was in good general health and had not lost any weight since the onset of the disease.

The patient came under my observation in May, 1926, at which time all the areas of previous involvement had again become active. The lesions in the mouth were particularly severe, the lips being greatly swollen and covered with closely

grouped flat pustules the size of a pinhead. On the inner sides of the cheeks and floor of the mouth, several grayish-white, rounded, slightly raised patches were present; vesicles or blebs were not observed; the patient had used the term "blisters" loosely; when carefully questioned, he agreed that blebs had never accompanied an outbreak. He complained of considerable pain, and deglutition was difficult; otherwise, there were no subjective symptoms, and the temperature and pulse were normal. During the following months, he seemed to improve under various local remedies, including wet dressings of sodium borate, boric acid, potassium sulphuret and mild silver protein. Mercuric chloride and mercurochrome-220 soluble were tried but even in weak solution caused considerable pain

Fig. 4 (case 2).—Active spreading lesions.

and inflammatory reaction. Injections of bismuth compounds and arsphenamine were given for a time, but did not seem to have any value.

Progress was slow; some of the lesions, especially those involving the mouth and genital region, persisted with but slight improvement. In September, 1927, the patient consulted Dr. Schamberg, who favored the diagnosis of dermatitis vegetans, but also called attention to the similarity morphologically to impetigo herpetiformis; on account of the lesions in the mouth, pemphigus could not be ruled out; yet when the benignity of the condition over a period of four years was considered, Dr. Schamberg was inclined to believe that local infection was the etiologic factor, and he had cultures made from the various locations involved. These cultures developed *Staphylococcus aureus*, which when tested with rats and monkeys gave negative results.

A

B

Fig. 5 (case 2).—April 27, 1928; *A*, circinate lesions coalescing and spreading peripherally; *B*, lesions on shoulder and back.

On Dr. Schamberg's suggestion, intragluteal injections of sodium arsenate were given, and a solution of potassium permanganate was applied as a wet dressing. Following this, remarkable improvement occurred; the lesions in the mouth and on the lips had subsided, and the lesion in the groin which had developed marked vegetations had practically disappeared. Early in November, the patient had a marked recurrence in all previous locations. His lips were greatly swollen and the mucous membrane in the location of the cheeks was covered with closely aggregated pustules. The feet, perineum and groins were likewise involved and were painful. The patient decided to try some "hydrotherapeutic plan" of treatment and was not seen again until April 27, 1928. His general condition at this time was unimpaired, and the lesions involving the mouth had practically disappeared; the lesions in the groin were also in a state of regression. An extensive circinate eruption, with active spreading, raised vesicopustular borders, had developed; it extended over the right shoulder, involved almost the entire chest on this side and extended down the back 5 or 6 inches (12.7 or 15.2 cm.). The middorsal region of the back was also involved; it showed the characteristic circinate lesions coalescing and developing large plaques with spreading, raised borders and elevated papillary pigmented centers. The patient had been receiving some form of light treatment and injections of "calcium."

It would be difficult to classify the conditions in the cases here reported under any of the grave constitutional dermatoses in which vegetations occur. If one considered the condition as pemphigus, the absence of bullae at any time and the lack of constitutional symptoms would argue strongly against this view. My conception of dermatitis herpetiformis with polymorphous lesions and intense pruritus is certainly unlike this condition. A clinical resemblance (in case 2) to impetigo herpetiformis in the early development of the lesions, before vegetations had formed was most pronounced, especially in comparison with the case described by Kaposi.[1] In this case, the disease had involved the pubic and adjacent genital regions, running out over the thighs. The lesions consisted of extensive erythematous areas with borders of closely grouped small pustules and disseminated circular lesions with erythematous bases and vesicopustular borders. Granting that there is a resemblance in the skin lesions, however, one would hardly be justified in placing them in this group, in view of the entire absence of any constitutional symptoms, which are the predominating feature in impetigo herpetiformis.

The problem of properly placing these cases seems impossible, unless one considers a special group.

In a brief review of some of the opinions advanced by those who reported cases of this type one finds that Pernet, after reviewing the cases of vegetating dermatoses that had appeared under various titles, including Jamieson's case of impetigo herpetiformis, Auspitz's case of herpes vegetans, Neumann's case of herpes pyaemicus and others, con-

1. Kaposi: Atlas der Hautkrankheiten, 2, Vienna, William Braumuller, 1899, plate 128.

cluded that his case corresponded morphologically with Hallopeau's rather than with any of the others; with this Radcliffe-Crocker agreed. Hartzell strongly opposed consideration of these cases as a type of pemphigus and felt that Hallopeau "had abandoned his early position too readily." In their report of a case under the title "dermatitis vegetans in its relation to dermatitis herpetiformis," Fordyce and Gottheil claimed an identity with Hallopeau's cases, but whether the condition was to be considered as an independent disease, a variety of pemphigus vegetans or dermatitis herpetiformis "was a question more easily asked than answered."

From the foregoing opinions, one can assume a definite agreement regarding the morphologic characteristics as outlined by Hallopeau; in addition to this, the long continued benign course of the cases reported, the lack of constitutional symptoms and the favorable response to local antiseptic treatment either in controlling the eruption or in effecting a cure would seem to warrant segregation until an etiologic factor is established or until more definite grounds can be advanced for considering a relationship to the grave constitutional conditions already considered. This could readily be done by placing them under a title defining the characteristic clinical manifestations, which is suggested in the case reported by Pernet and Radcliffe-Crocker.

The designation "dermatitis vegetans recurrens, Hallopeau" for these cases is hereby suggested for consideration.

ABSTRACT OF DISCUSSION

Dr. V. Pardo-Castello, Havana, Cuba: Dr. Wallhauser's cases remind me of a case of the same type I saw three years ago. The features were much the same, but the vegetating lesions were preceded by large bullae, which made me think of a diagnosis of pemphigus vegetans, but as the general health of the patient had been good for five years, that diagnosis was doubted.

I would like to know if sections of the tissue were made, and if blastomyces were looked for in the sections.

Dr. David King-Smith, Toronto: At the Congress in London in 1913, I presented a case in which I made a diagnosis of dermatitis vegetans, and it provoked much discussion. It was hard to decide whether the condition was dermatitis herpetiformis or pemphigus vegetans. I had the patient under observation for several years before reporting the case, and he lived for several years afterward. One of the features of this case was the presence of lesions in the mouth, and after the first year the patient developed vegetating lesions similar to those in the present case.

Dr. Walter J. Highman, New York: Dr. Wallhauser submitted a section of the tissue from the patient in case 1 to me, and the tissues from both this and the other case looked alike. Granulation tissue, which surgeons a century ago called "proud flesh," was the picture seen in the microscope. I think this corresponds roughly to the histologic picture of vegetating pemphigus. I do not think that dermatitis vegetans and pemphigus vegetans could be differentiated by histologic examination, but clinically it is obvious that there is no similarity between the

condition in the patients Dr. Wallhauser presented and pemphigus, in the accepted sense of the term today. The fact that some of the lesions which are observed might result from a pyogenic infection, whether bacterium or fungus, is obvious. Moreover, the mere presence of bullae in a case that otherwise runs a simple clinical course need not create alarm as to the possibility of pemphigus. Dr. Wallhauser has presented a sufficiently cleancut clinical entity, regardless of what he calls it, to make it worth while.

Dr. William Allen Pusey, Chicago: Dr. Wallhauser has done a good thing in directing attention again to this condition of dermatitis vegetans. I am not prepared to speak on all his cases, because some of them presented a new clinical picture to me, but one presented a rather closely analogous picture to Hallopeau's case and the cases reported by Hartzell and by me many years ago. My case certainly was not pemphigus, the differentiation being made on the basis of the broad essential differences and the clinical picture as well as the course. The lesions were exuberant granulations, fungating wildly, as Dr. Highman expressed it. The disease ran rather an acute course. The condition is analogous to kerion; it produces an intense inflammatory process that really kills itself. In my case, the condition was a combination of that in Hartzell's case and that in a case Wende reported. In Wende's case, the disease involved chiefly the face of a child, and in Hartzell's case the genital organs were involved. In my case, both of these areas were involved. The disease occurred in a dirty hostler, and under a regime of simple cleanliness and wet dressings the disorder quickly disappeared, leaving some hypertrophic scars.

I do not think the name should be changed. Dermatitis vegetans is a definite name. Names are nothing but labels, and constantly changing them to make them descriptive has been the source of the sad state of confusion in almost all nomenclature.

Dr. Howard Fox, New York: In one of the two patients who had previously been under my care, considerable changes had taken place since I had last seen him. I presented this patient before the New York Dermatological Society as having a possible case of pemphigus vegetans, a diagnosis that was thought by those present to be the most likely one. At that time, there were none of the circinate lesions which were seen in one of the photographs of Dr. Wallhauser. The presence of lesions in the mouth added weight to the probability of pemphigus, though it is true the patient was in good general condition and had not lost any appreciable amount of flesh and strength. He had been observed previously at Johns Hopkins Hospital, where Vincent's organisms were found in lesions of the penis as well as of the mouth, this condition being thought to be of etiologic importance.

Dr. Jay Frank Schamberg, Philadelphia: I had the privilege of seeing one of Dr. Wallhauser's patients, and whatever organisms were present were cultivated and inoculations made into rabbits, guinea-pigs and a monkey. All the cultures were negative. I agree with Dr. Wallhauser in the diagnosis of dermatitis vegetans (Hallopeau).

Dr. Wallhauser: Dr. Pardo-Castello's question relating to the microscopic examination was answered by Dr. Highman. I am in accord with Dr. Pusey as to restricting the wording of the title, but I feel that the addition of the term "recurrens" would seem warranted in calling attention to one of the main features in distinguishing these cases from those in which vegetations occur as secondary manifestations.

JEAN LOUIS ALIBERT *

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Alibert, the classic scholar, the brilliant speaker, the fascinating writer, the alert observer, the accomplished man of the world, was the happy means fate chose to initiate modern French dermatology.

Jean Louis Alibert was born in 1768, and died in 1837 at the age of 69. He was, therefore, 21 when the Bastile was stormed.

The French Revolution was not alone an economic and political upheaval but also a mental and moral reawakening. It has been said that then everything was young—the century, the government, the ideas, the modes of study and the subjects for study. The revolution was as profound in medicine as in other branches of thought, and an enumeration of some of Alibert's scientific contemporaries shows what a ferment was working in that busiest of capitals, Paris.

SOME OF ALIBERT'S CONTEMPORARIES

It was just fifteen years before the revolution that Priestley visited Lavoisier in Paris, and spoke to him of dephlogisticated air. Lavoisier made an investigation of its properties, named it oxygen and caused a complete revision of the language of chemistry. Hardly a day now passes with a physician, physiologist or chemist when he does not in some way have occasion to think of oxygen.

Then there was the brilliant Laennec, who not alone looked at his patients; he also examined them, and so introduced an epoch in medicine. He invented the stethoscope in 1815, and published his treatise on auscultation in 1819. Other men, following his example, also began to examine their patients, and to check up observations by postmortem examinations, and the consequence was definite ideas in regard to tuberculosis (Laennec and Louis), and diphtheria (Bretonneau). In the same hospital with Alibert, Marc Antoine Petit and his pupil, Etienne Serres, gave the first description of enteromesenteric fever, which Louis afterward so thoroughly restudied and called typhoid fever.

Contemporary with him in the hospitals of Paris were many whose names are yet familiar to us, such as Dupuytren (Dupuytren's contraction), Lugol (Lugol's solution) and Marjolin (Marjolin's ulcer). It was then also that Civiale invented an instrument, and performed the first crushing operation for stone in the bladder.

Under the old regimen, the teaching of medicine had become academically frozen, and quite apart from the definite case. As breaking the ice, Desault had established the first surgical clinic, and Corvisart the

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first clinic in medicine. Alibert had been the pupil of both these teachers, and, following their example, he began, on receiving an appointment to the Hospital Saint Louis, to use its rich material for teaching.

ALIBERT'S CAREER

Lucky Incidents.—As a youth, Alibert was employed in the teaching services of the church. When, during the revolution, these institutions were broken up and the state had to take over the service, Alibert continued as a teacher. In this way, he acquired an excellent classic and literary training which was exceptionally valuable to him afterward. The old medical faculty and institutions, completely antiquated, were also abolished, but medical men were a necessity. The armies of the republic alone required many surgeons, and the state medical service had to be reconstructed. When reconstructed it was new, alive and supervised by men of ability, who contributed to making the France of that period the leader in medicine and surgery. Alibert took up the study of medicine in Paris in 1794, at the age of 26, at the inception of this reconstruction period. His education had taught him to think in an orderly way, and had trained his natural facility of expression. His thesis for graduation, "A Dissertation on Intermittent Fevers," had a wide circulation, and secured him immediately a distinguished place, and the association with men who were rapidly advancing. In America there is a saying that opportunity comes more frequently than the ability to take advantage of it. Under the old regime in France, opportunity was reserved for the favored few, who usually disregarded it because it came so easily. During the revolution, this situation was reversed, and the conditions more resembled those in America. For instance, Napoleon's career and that of his marshals were only instances among thousands of a like nature.

As stated previously, Alibert secured control of a fine material at a time when French medicine was in the ascendency—the man and the hour had come. He had also the good fortune to write a book on diseases of the skin which had a wide sale. It was the first of its kind in which a Frenchman had addressed his readers in their own language. Even Lorry, the immediate predecessor of Alibert, had written in Latin. Not alone did Alibert write a book in the vernacular, but he illustrated it, which was also a great advance.

The Saint Louis Hospital.—In the Paris of the first days of the terror and of the revolution the famine forced people to eat decayed food, and the flesh derived from diseased animals. The city was crowded with the poor, the miserable and the starving. Those affected with disgusting skin diseases, such as the itch, and those suffering from incurable ulcers, were especially ticketed for the House of Grief called

the Saint Louis Hospital. It was about this time, also, that an outpatient department was instituted, with gratuitous treatment for the scrofulous, the scaly and the scabby.

It is said that evil and misery constitute the raw material out of which good is evolved, and it was out of this horror that dermatology, which has brought so many blessings to mankind, emerged.

In 1801, at the age of 33, Alibert received his appointment to the Saint Louis Hospital, and it was there that he functioned for so many years as the master and instructor for the dermatologists, not alone of Paris and of France, but of all Europe. When he began, he had at his disposal the greatest material then in the world,thrown together in the most disorderly fashion. All the ulcers, for example, were confounded together, whether they were syphilitic, tuberculous, leprous, streptococcic or even traumatic. For most of the material, the classification was eminently simple; the diseases of the head were called "tenia," and those of the rest of the cutaneous surface, "tetter." In addition to those, there were a number of other appellations, such as plica, ephilides, cancroids, leprosies, pians, ichthyoses, syphilides, scrofulas and psorides, but these seem to have been incidental, and scarcely made an impression on the inchoate mass of unknown uncharted conditions. Some of these terms have now fallen out of use, and others are more strictly defined, but it has taken years of time, immeasurable labor and the keenest intellect for observation and order to achieve the present classification. The weariness with the old teaching, the abundant and picturesque material and the personality of the lecturer secured Alibert an immediate and brilliant success.

The amphitheater in which he first met his pupils soon became too small to accommodate the great number of students, and especially of physicians, who came from all parts of Europe. This crowding was the primary reason for holding his sessions in the open air. As his classes were held at the end of spring and beginning of summer, the weather was usually fine, and the green fresh foliage, the blue sky and the birds accorded delightfully with the gay spirit of the lecturer.

He knew and was able to employ all the oratorical artifices. While considering the generalities of his subject, his voice became grave, full and harmonious, and his eloquence flowed out in cadenced periods. This even flow would be broken from time to time by an exclamation, an apostrophe or an antithesis. Latin citations alternated with Greek reminiscences, or ancient philosophers and modern authorities were invoked to clinch a point. If, on the contrary, he described the lesions pertaining to a case in hand, he assumed a conversational tone, and the phrases became shorter and more familiar. Each description was vivified by imagery and happy comparisons, together with recollections and anecdotes.

Only the rain obliged the participants to go indoors. Benches were placed for the audience under the lindens in the hospital grounds. The professor, with the patients at his side, occupied a platform of plain boards. In front of this, other patients were seated, carrying on their breast a placard with the name of the disease with which they were affected. At the side of the professor was hung a large picture of the celebrated tree of skin diseases, of which more will be told later. Behind him, on a line strung between two linden trees, were a number of illustrations. The professor himself, elegantly dressed in knee breeches and white stockings, his features in constant movement, and plucking incessantly at his cravat, kept up a running discourse on the disease in hand, diversified as indicated.

Alibert was able to secure a separate pavilion for dermatology, which contained a sufficient number of beds. Many an attempt was made by other departments to invade this sanctuary for the cutaneously afflicted, but Alibert was steadfast in his hold. Indeed, steadfastness was one of the marked characteristics of the man. Only once did he relent in his strict rule to allow only dermatologic patients in these wards, and that was under the terrible pressure of an epidemic of the plague. The storm having passed, however, he reverted to his former attitude. It is possibly through this influence that the chairs of dermatology on the continent of Europe, ever since the inception of the specialty, have held a more dignified place in medical teaching than they have been able to secure in the English speaking countries.

Like many of his contemporaries, Alibert began to study independently the individual case. And the individual case in his specialty was frequently so picturesque and often so grotesque as to accord well with his artistic temperament. In this way, he made notable contributions to the literature, as, for instance, the first descriptions of keloid, mycosis fungoides and sclerodermia and its varieties. His name also will always be associated indissolubly with the itch mite, although he himself did not discover it.

Classification.—Nothing could stop Alibert in his zeal in depicting or describing an interesting case. Once while an artist was painting for him an extremely horrible example, he had to assist personally, both in giving encouragement and also in providing abundance of vinegar water to overcome the horrible stench emanating from the patient's mouth. If, on the way to the hospital, he saw an interesting case, whether in a man or a woman, he made the sufferer be seated beside him in his beautiful carriage and conveyed him to the hospital to demonstrate the lesions to his audience. One day there appeared before him a man with well marked elephantiasis. "Fine," shouted Alibert. "Doctor, can I be cured?" "I shall have a painting made," continued the enthusiastic pro-

fessor. "But, doctor, may I hope for a cure?" "Certainly, certainly, but I wish a painting." "Can I get a bed in your service?" "If you needed ten, you could have them."

However, like every one who gathers a mass of knowledge and observation, he wished to classify his material. As before mentioned, he found already in use an eminently simple topographic classification, the tenias, or diseases of the head, and the tetters, or the diseases of the rest of the cutaneous surface. After many a mental struggle he ended by adopting an artistic classification, consisting of his celebrated "tree," with its branches.

The classification was artistic and fanciful, and accorded not at all with natural history and the facts of the subject. It, however, eminently suited the graphic inclinations of Alibert, and, as before mentioned, he had a copy hung on a tree while he delivered his lectures in the open air at the Saint Louis Hospital. There is also a beautiful cut of it in his celebrated atlas. When last in Paris, I was able to secure a fine copy of this atlas, at one time the property of the late Alfred Fournier. The tree is represented as being old, and the branches are broken. The bark is shaded in gold, and the vegetation at its foot in emerald green. Twined about the trunk is an emerald green snake holding in its mouth a cord, supporting a placard, as a sign that the trunk of the tree represents the skin and the main branches the diverse essential maladies. The small branches indicate the genera, and the twigs the species and varieties. Alibert himself was so insistent in introducing this tree, and his friends and enemies so often made it the subject of their jokes and sarcasms, that it finally assumed the position of his chief attribute, and nearly caused his good work and real merit to be forgotten.

There were other circumstances besides the ridiculous tree that nearly obliterated the memory and the essential worthiness of the man, the chief of which was the advent of a new classification, of which I shall speak later.

Practice.—Alibert's practice in the city of Paris itself, as apart from the court, was small, and justly so. He would discourse to a patient on art, literature, the news of the day, everything but the patient's case. It is doubtful if he were interested in the ordinary case. His patients came to him from all over the world on account of his world wide reputation.

Alfaric [1] divided his dermatologic life into three periods: The first was from 1801 to 1815; the second was between 1829 and 1837, and between these lay a third period of fourteen years, during which he gave up his hospital work and devoted himself to the service of royalty,

1. Alfaric, Achille: J. L. Alibert, Fondateur de la Dermatologie en France, Paris, 1917.

and in which he had the mortification to see arise in the Saint Louis Hospital itself a new school which bitterly fought his teaching, and nearly succeeded in causing him to be completely forgotten. Some of the incidents connected with this absence and return are so interesting as to be well worth recapitulating.

The middle period, mentioned previously, comprised that of the restoration of the monarchy subsequent to the battle of Waterloo; and it was a brilliant one for Alibert in regard to remuneration and social advancement, when he, through his position in the court, obtained a numerous clientele among the courtiers and the high state functionaries, suffering from a life of ease and plenteous living. In this brilliant assemblage of the victims of good fortune, Alibert showed himself to be adroit in relieving the troubles consequent on their impieties. He knew a great deal, and he knew how to apply his knowledge; he was good humored, enthusiastic and original. And finally, as an additional adornment to his natural charm and great learning, he received a title, a baronetcy, from Charles X, for his services to Louis XVIII.

It would appear that the special service touched an eczema on the royal legs. The reward is noteworthy, as few dermatologists have been so distinguished. Malcolm Morris, I believe, achieved his knighthood by clearing up an epithelioma of the eyelid of Edward VII, and I have heard him boast that he was the only English dermatologist so decorated for strictly medical services. Erasmus Wilson's knighthood was conferred, if I remember correctly, for spoiling, or rather despoiling, the Egyptians of one of their stone pillars, which he placed on the Embankment in London.

Alibert had office hours only on two days of each week, and maintained a magnificent suite of offices, which must have resembled a museum of art and natural history. There were collections of butterflies and insects from all over the world, and there were celebrated paintings of beautiful flowers placed side by side with plates of his great atlas representing ichthyoses, psoriasis, plica and other bizarre diseases.

Alibert and Biett.—Alibert had a favorite pupil named Laurent Theodore Biett, a Swiss, born in 1781, in Scamp, Canton Grisons (Graubuenden), who was, therefore, thirteen years younger than Alibert, enough difference to place him in another generation. Alibert was born in the south of France, and belonged temperamentally and geographically to the Mediterranean basin. Biett was born near the source of the Rhine, and belonged temperamentally and geographically to the North Sea tribes. Alibert was a Roman Catholic, both temperamentally and geographically, and Biett was a Protestant, both by temperament and birthplace. Biett was sober, severe and retiring, and in his demonstrations adhered strictly to the cutaneous manifestations and

facts. He was not the man for large generalizations and flights of fancy like Alibert, but he was clever enough really to contribute to the progress of dermatology, both in diagnosis and in treatment. He happened on a classification of diseases of the skin that suited his temperament exactly, and it was quite the opposite to the expansive artistic one adopted with enthusiasm by Alibert.

That these two men should form a strong friendship was remarkable. That they should teach the same subject in quite opposite ways was inevitable. A man to be natural must speak and act as his nature constrains him. That these different methods of teaching the same subject in the same institution would naturally lead to estrangement was in the course of events. Their friends alone would see to it that they were pitted against one another.

Willan's Classification of Diseases of the Skin.—In 1816, Biett had the good fortune to accompany a patient to England. After remaining for a time at the sea baths of Margate and Brighton, he went to London, where he visited Bateman's clinic, and became familiar with Willan's classification, a development of that of Plenk of Vienna. It was founded on the elementary pathologic manifestations, such as papules, pustules and wheals, and it suited, by its minutiae and its preciseness, the Biett type of mind. By paying attention to these manifestations Biett was enabled to make a formal and precise diagnosis, a circumstance highly satisfactory to a great number of people, and in marked contrast to the brilliant generalizations of Alibert. It used to be said that one went to Alibert's clinic to be amused, to that of Biett to be instructed. Such was the situation when Alibert returned from court life to regular visits to his clinic.

Alibert's Return to the Saint Louis Hospital.—Alibert returned to his work at the hospital after an absence of ten years. In the meantime many things had happened, and the world had changed. He was elderly, and he was pitted against a much younger man who had been steadily at work, and who was teaching the subject under a classification which, although faulty, conformed at least in a measure to natural history. Alibert, however, was enthusiastic, and entered on his work with his usual vim; he was determined that his tree should stand, and one of his main characteristics was tenacity of purpose.

The Tree.—For ages skin diseases had received botanic names. The eruptions (outbursts) were, and still are, called efflorescences (flowerings out), and individual diseases were called lichens (mosses) and mycoses (fungi), and for a man with Alibert's delight in words it was only a step from a botanic name for an individual disease to an entire botanic classification, so he took that step. In addition, Linnaeus, the Swedish botanist, a few years before, had published his classification

of plants, and it was so popular that undoubtedly it also exerted an influence. The tree appealed to Alibert because of its artistic quality, and he certainly made it a fine representation of a dead tree. Furthermore, in the Middle Ages, trees were a favorite means of classifying and illustrating all sorts of knowledge, including geneologic trees, and Alibert had many sympathies with the Middle Ages. His attachment to the church and to the monarchy showed that.

No one is ever entirely funny, unless in earnest, and Alibert was thoroughly in earnest, and exposed himself to the sharpest criticism, to the most biting sarcasm and to immeasurable ridicule in a city famous for practicing all these arts. Then there was the contrast with Biett, who had at least a workable classification. To the credit of both, neither indulged in personalities; each went his own way.

CONCLUSIONS

It is said that in his last illness Biett called on his old master. They had not met for years, and their estrangement, though silent, had been thorough. Alibert was deeply moved, and showed the greatest affection for his former pupil and associate. The man's nature was essentially kindly. Although his frivolities and light heartedness were immeasurable, his charity and benevolence were proverbial, and in a way sanctified the lighter features of his character.

Hardy described him in his last days as small in stature, with a round head covered by a brown wig, and a hat which appeared to be always on the point of tumbling off. Though aged, he still had a clear and harmonious voice and a quizzical smile. Up to the last, he was vivacious, imaginative and affable. His smiling philosophy had carried him through the revolution, the somber days of the terror, the directory, the consulate and the glorious empire, the evil days and the invasion of 1814, the paternal anarchy of the first restoration, the Hundred Days, the calm reigns of Louis XVIII and Charles X, the tragedy of July, 1830, and the bloody years following. He died in Paris, after a short illness, of cancer of the stomach, on Nov. 4, 1837, at the age of 69. He lived in the center of a storm such as had never been experienced in history, and passed through it without being embittered, or becoming negatively cynical. This was an achievement in itself.

It is not strange that such an impressionable man as Alibert should be horrified with the excesses of the terror, or that he should be attached to the colorful and picturesque features of the monarchy. Although a conservative, he always remained receptive to new ideas, both in politics and in science. In fact, in the latter he seems often to have been overenthusiastic. He had the gifts of memory, clear thinking and assimilation. He had the eye of a painter, and rapidly seized the objective

aspects and picturesque side of things, and he had the good fortune to become master of an immense congestion of material in the largest and best equipped hospital of the age. He had a clinical acumen that enabled him to pick out from this material examples of diseases which constituted new discoveries and to present his conceptions in such colorful language as to immortalize his name. He was often too pompous, and too desirous of producing an effect. But we all have seen pompous people with a less substantial backing; and desire for admiration and for producing a startling impression are sympathetic qualities.

THE HEMATOGENOUS PRODUCTION OF DERMATOMYCOSES

EXPERIMENTAL STUDIES *

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The fate of dermatophytes which have made their way into the organism interested observers long before it was known that they cause diseases of a general character. Beginning with the last decade of the past century, numerous authors (Quinke,[1] Elsenberg,[2] Truffi,[3] Citron [4] and others) attempted to elucidate the following points: 1. Are cutaneous fungi liable to vegetate in the visceral organs? 2. What toxic effects do they produce in such instances? The question also arose as to the rôle of the skin in cases in which fungi are introduced by way of the blood stream. For that purpose rabbits were inoculated intravenously, intraperitoneally or subcutaneously with cultures of *Trichophyton* or *Achorion* respectively, without, however, any resulting positive cutaneous or visceral lesions. In more recent publications, Bloch [5] emphatically stated that the subcutaneous or intravenous ways of infection with fungi do not immunize or reproduce the disease in animals. Lombardo,[6] too, failed to produce allergic reactions in instances in which *Trichophyton* entered the body in a way other than through the skin.

Sabrazés,[7] however, described miliary granulations found in the lung of one rabbit, in a series of subcutaneous and intravenous infections with *Trichophyton* and *Oospora canina*. The lesion in this case was mostly

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1. Quinke, H.: Zur Favusfrage, Arch. f. Dermat. u. Syph. **31**:65, 1895.

2. Elsenberg, A.: Ueber den Favuspilz, Arch. f. Dermat. u. Syph. **21**:179, 1889.

3. Truffi: Richerche Sperimentali sulla tigne, Gior. ital. d. mal. ven. **43**:67, 1902.

4. Citron, J.: Ueber das Verhalten des Favus und Trichophytonpilze im Organismus, Ztschr. f. Hyg. u. Infektionskrankh. **49**:120, 1905.

5. Bloch, Bruno: Zur Lehre von den Dermatomykosen, Arch. f. Dermat. u. Syph. **93**:157, 1908.

6. Lombardo, C.: Richerche sulla ipersensibilità ed immunità in alcune dermatomicosi, Gior. ital. d. mal. ven. **52**:70, 1911.

7. Sabrazés, J.: Favus de l'homme, de la poule et du chien, Ann. de dermat. et syph. **4**:340, 1893.

intravascular, being composed of leukocytes and centrally located mycelial filaments. Bukowský,[8] who injected into the veins of rabbits 1 cc. of an emulsion of the culture of *Achorion*, found that the heavier the emulsion is the sooner the animal dies; and that if weak concentrations are used the animal does not show any clinical deviation from normal. By histologic examination of the organs, he, too, found miliary granulations composed of leukocytes and vegetating fungi. None of the authors were able to reproduce a cutaneous lesion by using the hematogenous way of infection.

In 1916, Saeves[9] reproduced for the first time cutaneous lesions in a guinea-pig infected intracardially with *Trichophyton gypseum* and *Achorion quinckeanum*. This author applied the method of Lewandowsky, who reproduced cutaneous tuberculids in animals which were infected intracardially with Koch's bacillus, and in which the skin on the belly was previously shaved. In 1916, Kogoj[10] verified and broadened the experiments of Saeves.[9] He was able to reproduce cutaneous dermatoses by injecting emulsions of spores of *Achorion quinckeanum* into the lumbar sac, the subarachnoid spaces, the testicles and the liver. He found lesions in the scarified as well as in the intact areas of the skin, although in the former the lesions were more pronounced and their appearance was more precocious. Kogoj[10] quoted a few authors who failed to reproduce skin lesions by using the intravenous way. He, himself, did not produce infection in animals by way of the blood vessels. Saeves explained the failure of previous authors to produce skin lesions by using the intravascular way on the basis of the inadequacy of the methods employed, on the variations of the virulence of the fungi and, finally, on the concentration of the emulsified material.

The general biologic interest of hematogenous infection, on the one hand, and some obscure points concerning the localization of the fungus, on the other, have led us to undertake a series of new experiments dealing with this method of reproducing cutaneous lesions.

EXPERIMENTS

We used a culture of *Trichophyton gypseum*, from 2 to 3 months old, which was isolated from a patient with a deep trichophytosis two years before the experiment. The culture was passed many times through a guinea-pig and also was reinoculated on Sabouraud's dextrose-agar medium from twelve to twenty-one times. The whole culture from one test tube was then emulsified in 20 cc. of physiologic sodium chloride solution and filtered on six or seven layers of cheese cloth. The

8. Bukowský, J.: Ein Beitrag zur Kenntnis der experimentellen und klinischen Eigenschaften des Achorion schönleinii, Arch. f. Dermat. u. Syph. **51**:365, 1900.

9. Saeves, I.: Experimentelle Beiträge zur Dermatomykosenlehre, Arch. f. Dermat. u. Syph. **121**:161, 1916.

10. Kogoj, F.: Experimentelle Beiträge zur Lehre von den Dermatomykosen, Arch. f. Dermat. u. Syph. **150**:331, 1926.

opalescent filtrate thus obtained showed under the microscope (Zeiss, objective 30, ocular X 3) from thirty to fifty spores in the field.

The experiments were conducted on rabbits. The intravenous method was used in the majority of experiments. Previous to the experiments, an area of from 10 to 15 cm. on the back or on the side of the animal was shaved and scarified with sandpaper. The animal was thoroughly wrapped in a blanket so that the ear only was exposed. Amounts varying from 2 to 5 cc. of the emulsion were introduced into the marginal vein of the ear; the wound was then cauterized, and the whole ear thickly painted with iodine. The animal was placed in a separate cage where animals with dermatoses had never been kept previously.

Twenty-nine animals were used in the experiments. Eleven, or 38 per cent, gave a positive result. The following examples are illustrative of the whole series of experiments.

RABBIT 1.—Sept. 27, 1926. The animal was shaved and scarified in the manner indicated, and 2 cc. of an emulsion of *Trichophyton gypseum* was injected into the heart.

Dec. 10, 1926: A few foci varying in size from 3 mm. to 1 cm. were disclosed on the shaved area. Hyperemia, slight edema and also scaling were present. The scales contained fungi.

Dec. 18, 1926: There was a pronounced edema of one focus. Numerous hairs were infected.

Dec. 25, 1926: Some foci were covered with crusts. New foci appeared.

Jan. 15, 1927: Most of the foci had fused, forming one infected spot, measuring 2 by 5 cm. This was markedly hyperemic and contained numerous grayish-white scales. Pronounced edema was present.

Jan. 28, 1927: Small crusts were found in the central part of the lesion only.

Feb. 2, 1927: The skin showed almost a normal aspect.

RABBIT 2.—Sept. 27, 1926: The left side of the animal was shaved and scarified in the usual manner. Two cubic centimeters of an emulsion of *Trichophyton gypseum* was introduced into the marginal vein of the ear with the precautions already noted.

Dec. 11, 1926: The shaved area showed the presence of scales. A focus about 1 cm. in diameter was present; fungi were found in the hair and also in the scales.

Dec. 17, 1926: The focus was spreading. There was a considerable hyperemia and numerous infected hair.

Dec. 27, 1926: A new focus appeared on the shaved surface with abundant scaling.

Dec. 31, 1926: The entire shaved area was covered with multiple foci.

Jan. 15, 1927: The small foci had fused. The entire infected region was infiltrated, and its central part raised above the surface of the skin.

Jan. 28, 1927: In the center, the skin began to show a normal aspect. At the periphery, the disease had not yet subsided. Fungi were present.

Feb. 10, 1928: The skin was almost clear, and hair was beginning to grow.

RABBIT 3.—Oct. 6, 1927. The hair was clipped and the skin scarified. Five cubic centimeters of an emulsion of *Trichophyton gypseum* was introduced into the the blood by way of the vein.

Oct. 18, 1927: A small focus measuring about 5 mm. appeared on the clipped surface of the skin. Scaling and fungi were present.

Oct. 25, 1927: The focus was hyperemic. There was a slight infiltration.

Nov. 20, 1927: The focus measured 1.5 cm. in diameter. There was a marked hyperemia but no infiltration. The hair of the scarified area fell out (alopecia).

Nov. 26, 1927: The disease began to disappear. Hair began to appear.

RABBIT 4.—Oct. 6, 1927: Clipping of the hair was followed by scarification. An intravenous injection of 5 cc. of an emulsion of *Trichophyton gypseum* was made.

Oct. 23, 1927: A marked scaling of the whole scarified area occurred. There was no hyperemia or infiltration. The hair contained scales and fungi.

Nov. 1, 1927: Scaling occurred. Fungi were present.

Nov. 10, 1927: Scaling occurred, but no fungi were disclosed in the scales.

Nov. 25, 1927: The center of the scarified skin began to take a normal aspect. Hair began to grow.

COMMENT

The Cutaneous Localization of the Parasite.—The four examples cited, which as we have said, are typical of the entire series of experiments, show clearly the character of the lesion in instances in which the fungus is introduced into the blood by way of the veins. From the experiments, it will be seen that the lesion in all animals appeared only in the scarified area of the skin. In one instance a diseased focus appeared in a nonirritated region, but close investigation showed that it developed on a traumatized spot due to a bite. Kogoj noted the appearance of foci on the surface of the ear where this structure was punched by a wire to attach the identification plaque. In our series, this was performed one month previous to the experiments, and probably due to that fact no local lesions were observed. The incubation period in the experiments herein presented varied from twelve to eighteen days, which is much longer than that seen in ectogenous infection. The character of the lesion varied from animal to animal. In some instances, there was alopecia with scaling and the presence of fungi in the scales; in other instances, there were isolated foci with fine scaling and hyperemia; and in still others, the lesion was diffuse, being covered with crusts occupying the whole scarified area. The disease lasted from six to twelve weeks. It also appeared that the amount of material injected did not influence the character of the lesion. Thus, rabbits 1 and 2, which received 2 cc. of the emulsion, were more seriously ill and their illness lasted longer than that of rabbit 4, which received intravenously 5 cc. of the same concentration. Apparently the host himself, other conditions being equal, is of paramount importance. It is also probable that the manner in which the animal was prepared (clipping or shaving) plays a rôle in the development of the disease. In no instance did we notice the appearance of general symptoms, such as loss of weight or of appetite, in the animals.

The localization of the lesion is of interest, indeed. Saeves, whom we have already quoted, attributed the failure of previous workers to produce skin lesions with the intracardial way of infection to the fact that the infectious material had probably not entered the heart. But Kogoj,[10] as we have already said, was able to cause a skin disease in animals that received the fungus into the lumbar sac, into the cranium,

etc. In a recent study by French workers,[11] positive cutaneous lesions were induced in rabbits by feeding them with the fungus by mouth or by injecting it into the peritoneum. These authors used our own method of shaving and scarification of the skin.

Still less convincing is the argument that a cutaneous lesion could not be reproduced because of the insufficient amount of material injected. In the experiments herein described, we used from 2 to 5 cc. of the emulsion with the positive results noted, without causing any disturbance to the animal. It is interesting that Bukowský and Sabrazés, dealing with sufficiently virulent strains of *Achorion* and *Trichophyton,* caused death of the animals by injecting the same amount of material without producing cutaneous lesions.

Apparently the shaving and scarification of the skin preceding the inoculation are responsible for the success of recent workers. In none of our experiments did we notice the appearance of lesions in areas in which the skin was not prepared previously. It is difficult to ascertain whether trauma of the skin per se (scarification), causing a locus minoris resistentiae, leads to the confinement of the disease to this particular area. Tarnowsky,[12] for instance, was able to provoke a local specific cutaneous lesion in a person with latent syphilis by previously cauterizing this region of the skin. Scherschewsky and Worms also obtained similar results by scarifying some cutaneous spot. It is possible that besides the locus minoris resistentiae in the experiments here reported, the elective rôle of the fungus toward the skin played a part in the causation of a dermatosis.

In brief, then, the localization of cutaneous lesions by the intravenous injection of fungi can be plausibly explained as follows: When introduced into the blood, *Trichophyton* remains in the circulation for a certain period of time. In instances in which the skin is intact, the normal wall of the cutaneous capillaries serves probably as a barrier interfering with their "diapedesis" and therefore with the ultimate formation of a skin lesion. Shaving scarification or any other factor leading to local inflammation favors the migration of the parasite from the papillary capillaries into the skin where it develops its pathogenic properties.

The Persistence of the Parasite in the Blood.—In his experiments, Kogoj stated that cutaneous lesions occur only when the skin is scarified twenty-four hours following the inoculation of the parasite. He consequently expressed the belief that the spores disappear from the blood rapidly. To elucidate the question, we have performed a series of investigations with blood cultures from the infected animals. The blood

11. Brocq-Rosseau, Urbain and Barotte: Sur i'électivité cutanée des teignes animales, Comp. rend. Soc. de biol. **95**:966, 1926.

12. Tarnowsky, quoted by Kogoj (footnote 10).

in these experiments was taken from the heart. Minute, aseptic precautions were taken to avoid contaminations with the fungus. From six to eight test tubes containing Sabouraud's dextrose-agar and dextrose-bouillon, respectively, were inoculated. It is interesting that the solid culture gave more positive results than the liquid. This is possibly due to the fact that the strictly aerobic parasite did not get enough oxygen in the bouillon. The accompanying table shows the results obtained.

From the table, it will be seen that in three of six rabbits the blood was still positive twenty-eight hours after inoculation, and in one instance it contained a pure culture of *Trichophyton gypseum* seventy-two hours after the infection of the blood. It is, however, noteworthy that the bulk of the parasite disappeared from the blood within twenty-four hours. Jessner and Hoffmann expressed the belief that there is an accumulation of immune bodies in the blood of patients with trichophytosis. It is then possible that the parasite disappears, being "driven"

Results of Blood Cultures

Hours After Infection	Number of Animals	Positive Results	Negative Results	Number of Tubes Inoculated	Positive Results	Negative Results	Positive Percentage
1 hour. 15 minutes.	2	2	0	14 tubes, 2 flasks	14+2	0	100
3 hours	2	2	0	15 tubes	15	0	100
5 hours	1	1	0	7 tubes, 1 flask	7	1 flask	100
28 hours	6	3	3	41 tubes, 2 flasks	4	32 tubes, 2 flasks	10
46 hours	3	1	2	20 tubes	1	19	5
72 hours	8	1	7	52 tubes	1	51	2

from the blood by the immune bodies. This, however, requires further investigation.

Another interesting phase of our investigation with blood cultures is as follows:

Jadassohn [13] affirmed that parasitic elements originating from a *Trichophyton* focus penetrate into the follicle from the outside through the opening in the skin. In support of his idea, he brought forward the following facts: (1) the frequent appearances of Trichophyton in the neighborhood of the kerion; (2) the finding of fungi in the lichenoid elements of the patient's skin. Pedersen,[14] however, has shown by using the intradermal reaction that the cutaneous allergy is more marked in the proximity of the primary focus. As regards the presence of fungi on the affected skin, it is noticeable that it is more frequently seen in microsporosis than in deep trichophytosis; however, microsporosis is seen much more often than trichophytosis. On the contrary, one has

13. Jadassohn, W.: Beitrag zur Genese der Allergie bei Impfmykosen, Arch. f. Dermat. u. Syph. **153**:476, 1927.

14. Pedersen, B.: Ein Beitrag zum studium der Pathogenese der secundären Trichophytide, Dermat. Ztschr. **24**:731, 1917.

great difficulties in disclosing the parasite of deep trichophytosis even in the focus itself. It would appear that recent theories of hematogenous fungus infection explain more plausibly *Trichophyton* or *Microsporon* infections. The isolation of pure cultures of the parasite from the blood of patients with *Trichophyton* disease reported by Ambrosoli,[15] Jessner,[16] Passini [17] and Sutter [18] furnishes a key to the better understanding of the mechanism of the genesis of the trichophytoses.

SUMMARY AND CONCLUSIONS

In rabbits, an area of skin from 10 to 15 cm. in diameter was shaved or clipped and subsequently scarcified with sandpaper. From 2 to 5 cc. of an emulsion of *Trichophyton gypseum* was then injected intravenously into the animals. Of the twenty-nine animals used in the experiments, eleven, or 38 per cent, developed cutaneous lesions confined to the shaved and scarified areas only.

The confinement of the lesion to the skin in these experiments is due apparently to trauma of the wall of the papillary capillaries, which permits the parasite to "migrate" into the skin, where it manifests its pathogenic properties.

The intravenously introduced parasite circulates in the blood for not less than three days, although the bulk of the fungus disappears from the circulation within the first twenty-four hours.

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15. Ambrosoli, G. A.: Coltura di trichophyton Gypseum del sangue circolante in trichofizia profonda con lichen trichophyticus, Gior. ital. d. mal. ven. **62**:233, 1921.

16. Jessner, M.: Zur Pathogenese der Trichophytide, Arch. f. Dermat. u. Syph. **136**:416, 1921.

17. Passini, A.: Zur Trichophytonkultur aus dem zierkulierenden Blute bei Trichophytiden, Arch. f. Dermat. u. Syph. **140**:369, 1921.

18. Sutter, E.: Zur Kenntnis der Pathogenese der Trichophytide, Arch. f. Dermat. u. Syph. **127**:735, 1919.

MERCURIC SALICYLATE

A STUDY OF ITS EXCRETION IN THE TREATMENT OF SYPHILIS *

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Mercuric salicylate was first recommended as a syphilitic remedy in 1887 by Silva Arranjo of Brazil. Because of its comparative painlessness by intramuscular injection, its use spread rapidly, so that it has probably been more widely employed than any other preparation of mercury. Moreover, it has been a comparatively safe remedy as compared with other salts of this metal. Study of the 108 fatalities reported as resulting from the use of mercury from 1883 to 1901 [1] shows that 7 of the deaths were from soluble injections and 78 from insoluble injections of different mercurials. Mercurial oil was the cause of 31 of these, mild mercurous chloride of 8, and although mercuric salicylate was probably used far more than any other, it was the cause of only ten deaths. Lomholt says that during his experience two deaths have resulted from the use of this salt. In our clinic at Cleveland we have used mercuric salicylate for years, employing a 20 per cent suspension, in thousands and thousands of injections, without a single fatality.

From the therapeutic standpoint, there has always been considerable difference of opinion in regard to the use of mercuric salicylate. Thus Stokes,[2] in his Modern Clinical Syphilology, writes: "While mercury salicylate has an immense popularity, the users should realize that its relative efficiency in the treatment of syphilis is not determined,

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* The expenses of this investigation have been met mainly by the Lakeside Hospital, and by a grant from the Therapeutic Research Committee of the Council of Pharmacy and Chemistry of the American Medical Association.

1. Wolkenstein: Berl. klin. Wchnschr. **50**:1904, 1913. Neubeck: Dermat. Ztschr. **9**:470, 1902.

2. Stokes, J. H.: Modern Clinical Syphilology, Philadelphia, W. B. Saunders Company, 1926, p. 147.

and has been seriously questioned." He quotes Nelson and Anderson [3] who rather unsystematically treated forty-three patients with latent and seven with secondary syphilis in a penitentiary. Their dosage was 1½ grains (0.09 Gm.) once a week in the beginning and then every fourteen days; later it was given irregularly. It is not surprising that their results were nil. Best [4] criticized their results and reported that he had obtained good clinical results in ten cases in which the patients were treated once a week, with from ten to twenty-five injections, averaging twenty injections. He states "that he had found mercury salicylate injections the most convenient, the most easily controlled, the most efficient and the most satisfactory of any of the various forms of mercury treatment." Goodman,[5] with his rather meager statistics, found its results favorable. Haller [6] thought it had an influence on the Wassermann reaction in addition to its clinical effects. Kroeff,[7] from an experience with more than 8,800 injections, also confirms its clinical value. He said that only one abscess resulted from the entire number of treatments. Von den Porten [8] thinks that mercuric salicylate is too weak, but Jadassohn,[9] in his "Outline of the Modern Methods for Treating Syphilis," recommends it as a suitable mercurial. Recently Smechula [10] from Stümpke's clinic compared the results of treatment in fifty cases of secondary syphilis and in fifty of latent syphilis in which the patients were treated with neoarsphenamine and mercuric salicylate with fifty similar cases of each in which the patients were treated with neoarsphenamine plus bismuth emulsion. The serologic results were more favorable with the patients treated with mercuric salicylate. In contrast to this, Hill and Young [11] working with syphilis in rabbits found lesions developing during mercuric salicylate therapy, and spirochetes still flourished in the lesions. They did not think the results were so good as with the cyanide or with the biniodide, and that it did not compare with the action of flumerin. This corresponds to Stokes' remarks that he had seen patients under treatment with mercuric

3. Nelson, K., and Anderson, E. A.: The Use of Mercury Salicylate in Syphilis, J. A. M. A. **65**:1905 (Nov. 27) 1915.

4. Best: M. Rec. **89**:473, 1916.

5. Goodman, H.: Effects of Mercury Salicylate on Wassermann Reaction, Arch. Dermat. & Syph. **2**:193 (Aug.) 1920.

6. Haller, D. A.: Wassermann Variations, J. A. M. A. **66**:882 (March 18) 1916.

7. Kroeff, M.: Brasil-med. **2**:117, 1922.

8. Von den Porten, P.: Dermat. Wchnschr. **81**:1811-1812, 1925.

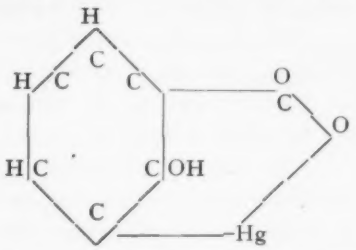
9. Jadassohn, J.: Deutsche. med. Wchnschr. **48**:19, 1922.

10. Smechula: Klin. Wchnschr. **4**:1493, 1925.

11. Hill, J. H., and Young, H. H.: Experimental Studies with Mercurials in Experimental Syphilis, J. A. M. A. **80**:1365 (May 12) 1923.

salicylate develop condylomata lata swarming with *Spirochaeta pallida*. This applies, however, to the other mercurials under certain circumstances, as all syphilologists can testify. It is evident from these contradictory quotations that mercuric salicylate requires further careful investigation in the clinic as well as in the laboratory. As one feature of this, a study of its absorption, fate in the body and excretion appeared desirable.

As pointed out by Dimroth,[12] mercuric salicylate is an anhydride of ortho-oxy-mercuri-salicylic acid. Lomholt [13] raises the point that



only one of the two valences of the divalent mercury is connected to the carboxyl of the acid. The other is directly connected to the carbon of the benzene nucleus. This, he says, produces a compound difficult of decomposition. He feels that undoubtedly a considerable quantity of the remedy is eliminated from the body without liberating its mercury. Because of this, he does not think mercuric salicylate could be an absolutely reliable remedy.

The absorption was investigated directly by Schamberg, Kolmer and Raiziss [14] on a rabbit given intramuscular injections with 180 mg. of mercuric salicylate, corresponding to 104 mg. of metallic mercury. When it died forty-five days later, they recovered 48 mg. of mercury from the site of the injection; therefore, 46 per cent was unabsorbed. From this they calculated the average daily rate of absorption in this rabbit as 1.2 per cent; but such an average does not have any meaning, since the absorption is much greater at the beginning than at the end. Lomholt observed the following results on a rabbit when it was killed after it had been watched for nine days: The total amount of mercury injected was 38.5 mg.; 9.88 mg. was excreted through the kidneys and feces; at autopsy, 3.10 mg. was found in the entrails, 6.4 mg. in the body generally and 11.54 mg., or 30 per cent, in the area of injection. The loss was 2.6 mg. In other words, about 70 per cent was absorbed in nine days, and about 25 per cent was excreted. The results harmonize with those obtained in our roent-

12. Dimroth, O.: Ber. d. deutsch. chem. Gesellsch. **35**:2853, 1902.

13. Lomholt, S.: Arch. f. Dermat. u. Syph. **126**:1, 1918; Brit. J. Dermat. **32**:353, 1920.

14. Schamberg, J. F.; Kolmer, J. A., and Raiziss, J. W.: J. Cutan. Dis. **33**:819, 1915.

gen-ray study on the absorption [15] of injections of mercuric salicylate into the gluteal muscles of human subjects. With these, the x-ray shadow disappeared in a mean of four days, and in extremes of from four to ten days; from the lumbar muscles it disappeared in a mean of six and a half days, with extremes of from two to beyond twenty-four days.

In human beings, the excretion of mercuric salicylate was studied chemically by Winternitz [16] in 1889. The methods used were rather crude and related only to the urinary excretion, but they sufficed to show that there was a comparatively rapid excretion of the drug. In 1906, Bürgi [17] using the Farup method of estimation, studied the patient's urine every two hours after an injection of 0.1 Gm. of mercuric salicylate. In four hours, the patient had already excreted 2 mg. of mercury. In another four hours, 1.25 mg. of mercury was excreted; in the next two hours, 1 mg.; in the next four hours, 1.5 mg.; and by the next morning, only small amounts of mercury were being excreted. The experiment illustrates the rapidity of excretion. Another patient on the same dosage showed a high excretion level (7 mg.) on the day after the injection; this dropped comparatively rapidly on the following day and a respectable amount of the mercury was still being excreted at the end of a week. For another of Bürgi's patients, a curve was made showing the excretion level following the end of a course of ten injections of mercuric salicylate, 0.1 Gm. being given the day before the beginning of the observation. The patient was observed for thirty-four days, when another injection of 0.1 Gm. was administered. The curve at the beginning showed an excretion of 6.5 mg. It stayed over 3 mg. for the next four days, and then dropped to 1 or 1.5 mg. for about a week, and from then on to the thirtieth day it varied between 0.5 and 1 mg. There was almost nothing for three days; then an increase occurred with the new injection. From this interesting experiment by Bürgi, it appears that despite the rapid initial excretion of the drug, there is, nevertheless, in a series of injections, a certain amount of accumulation which continues for a period of time after the last treatment. This corresponds to the view of Welander and Winternitz. Bürgi, using a vegetable oil base, found the excretion level for the mercury higher than that of Buchtala,[18] who used a paraffin base.

In our own experiments, the patients were put on a foreperiod of two days, in order to confirm the fact that mercury was not present

15. Cole, H. N.; Littman, S., and Sollmann, T.: Study of Mercury Injections by Means of Roentgen Ray, J. A. M. A. **75**:1559 (Dec. 4) 1920.

16. Winternitz: Arch. f. Dermat. u. Syph. **21**:783, 1889.

17. Bürgi: Arch. f. Dermat. u. Syph. **79**:1, 1906.

18. Buchtala, H.: Ztschr. f. physiol. Chem. **83**:249, 1913.

in the system. Then an injection of 1 cc. of a 10 per cent mercuric salicylate in a vegetable oil suspension (about 60 mg. of metallic mercury) was given. One of the patients was given the first injection at 4:30 p. m.; the others, at 1:30 p. m. Consequently, it was necessary to adjust our computations until the next day at 4:30 or 1:30 p. m., respectively, and thereafter from 7:30 a. m. to 7:30 a. m. The first day the collection of urine was made one, two, four, eight, sixteen and twenty-four hours after the injection, and thereafter every twenty-four hours until the time of the next injection. The feces were taken daily, and each sample was analyzed separately. One of the patients was given only one injection; two received four injections each, and one, five injections; all injections were given at intervals of a week. After the last injection, there was an after-period of as long as it was possible to observe the patient. The results were charted in several ways: (*a*) in terms of hourly excretion of urinary mercury and volume of urine; (*b*) daily excretion of mercury and urine, and (*c*) cumulative excretion of urinary mercury. The analysis of these curves showing the amount of excretion reveals several interesting phenomena.

RAPIDITY AND RATE OF THE EXCRETION

Chart 1 shows that mercuric salicylate is excreted rapidly, confirming the observations of the other investigators. Following the first injection given our four patients, the hourly excretion during the first hour was 0.16, 0.18, 0.19 and 1.13 mg., respectively, with a median of 0.185 mg. of metallic mercury. During the second hour, the excretion ran 0.18, 0.28, 0.56 and 0.69 with a median of 0.42 mg. Between the second and fourth hours, it fell somewhat, to 0.13, 0.27, 0.3 and 0.51 with a median of 0.285 mg. of metallic mercury per hour.

In sixteen hours, however, the rate had already dropped to 0.085, 0.09, 0.102 and 0.26 and a median of 0.096. For the succeeding days, the hourly excretion rate dropped further; on the second day, to 0.028, 0.05 and 0.055; on the third day to 0.02, 0.028 and 0.04; and by the sixth day, to 0.012, 0.027 and 0.027 mg. of metallic mercury.

When a new injection is made, one notes once more a rapid rise; even for the first hour, the hourly rate of excretion is 0.18, 0.19 and 0.33 mg. of metallic mercury. By the second hour, the hourly rate rises to 0.24, 0.48 and 0.92 mg. of metallic mercury. This rate falls rapidly, so that by the twenty-fourth hour it reads 0.09, 0.097 and 0.15. On the succeeding eighth, ninth, tenth and eleventh days, there is the same drop as during the first week, though it does not run so low; so that by the twelfth day, for example, it is 0.014, 0.025 and 0.066 mg. of metallic mercury. There is thus a slight cumulative increase in the

excretion of mercury as the curve progresses. With the third injection, there is again a tendency for a rapid rise in two of the patients, up to a rate of 0.45 and 0.36 mg., and during the third week the gradual cumulation of mercuric salicylate is more noticeable. Whereas on the third day of the first week, the rate of excretion for the three patients was 0.02, 0.028 and 0.04 mg., on the third day of the second week, it was 0.040, 0.048 and 0.62 mg. and on the third day of the third week, it was 0.11, 0.123 and 0.17 mg. With the fourth injection there was again a rapid rise in all three patients, but only one showed a higher rate than that following the third injection. It appears,

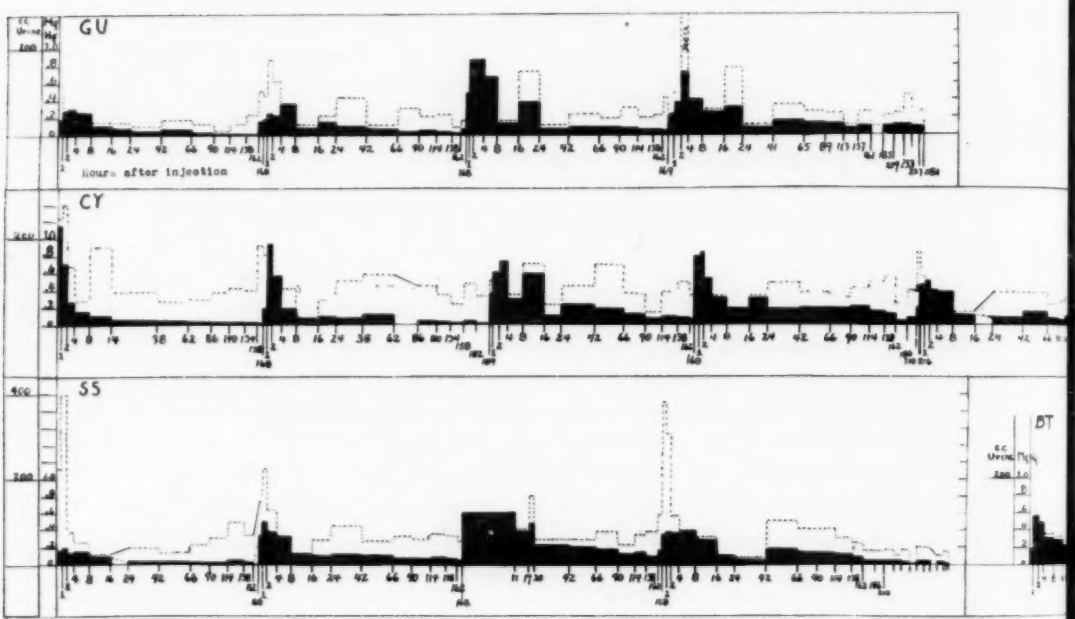


Chart 1.—Hourly excretion of urinary mercury (mg.) and volume of urine. The heavy black indicates metallic mercury in milligrams. The dotted line indicates excretion of urine in cubic centimeters. The injections were given in the afternoon; the time is plotted logarithmically.

therefore, that the rate of excretion of mercury and the volume of urine rise progressively after the first three injections, and then sharply fall after further injections. This phenomenon seems also to have been present in Bürgi's case. Lomholt's curve could not show this phenomenon, as the same dose was not used with each injection. We are inclined to believe that these changes may be explained as the result of a mild nephrosis following the irritation of the mercury, and causing first an increased and then a diminished permeability of the kidneys to mercury. Is not this the answer to the occasional micro-

scopic red blood cells seen in the urine of patients receiving mercurial injections?

In no case did we follow the patient after the first or last injection for as long a period as Bürgi. Nevertheless, after the last injection given to patient G. U., at the end of thirty-four days after the first injection and thirteen days after the fourth injection, there was still a rate of excretion of 0.07 mg. of mercury per hour and a total excretion of 1.62 mg. of metallic mercury per day. After the fifth injection, at the end of forty-one days, and nine days after the last injection given to C. Y. there was still a rate of excretion of 0.138 mg. per hour and a total of 3.3 mg. of metallic mercury; after forty-two days, and twenty days after the last injection given to S. S. there was a rate of excretion per hour of 0.025 mg. and a total daily excretion of 0.6 mg. of metallic mercury.

In other words, after a course of mercuric salicylate there is an appreciable excretion of mercury for some time after the administration of the drug has been stopped, even when only five injections are given. Whether this mercury is in a form that is therapeutically effective is another question.

TOTAL DAILY EXCRETION OF MERCURY

The individual curves showing the daily excretion of mercury and urine are shown in chart 2. They again illustrate the rapid elimination of the mercuric salicylate and confirm the observations of Bürgi, of Lomholt, of Winternitz, of Welander and others.

After the first injection, the excretions during the first day were 1.90 in eighteen hours, 3.53 in twenty-four hours, 3.61 in sixteen hours and 6.64 mg. of metallic mercury in twenty-four hours. This dropped abruptly on the second day (or more exactly between the twenty-fourth and the forty-second hour) to 0.86, 1.16 and 2.64 mg. and to 0.30, 0.57 and 0.66 mg. by the sixth day. In all the cases, the rise following the second injection was greater than after the first: 3.8, 4.12 and 4.51 mg. Here again, however, we begin to notice a gradual cumulative rise during the following days. The excretion after the third injection was far higher in all three cases than that after either the first or second injection. It reached a total of 9.05, 9.31 and 9.66 mg. of metallic mercury. These figures compare well with those of Lomholt, who had one patient whose excretion of metallic mercury increased to 11.17 mg. After the third injection, however, as we have already discussed in the paragraph on the hourly rate of excretion, in two of the patients the total amount of mercury excreted gradually fell, and in only one of these cases did the amount rise to a greater height after the fourth injection than it had after the third. This amount was not sustained, however, and in the end was not as much

as that after the third injection, as can be seen by comparing the charts showing the excretion per hour. The increased rate of excretion following mercuric injections is brought out strikingly by the cumulative excretion curves in chart 3.

The curves indicate that after an injection of mercuric salicylate, there seems to be one portion which is rapidly assimilated into the blood stream and excreted. This portion may reach a height of 1.1 mg. during the first hour, or 9.66 mg. for the first day after the injection. The other portion of the mercuric salicylate is more slowly absorbed, perhaps because it is incorporated in an oil vehicle. At any rate, it is this portion that seems to show a cumulative curve as the injections

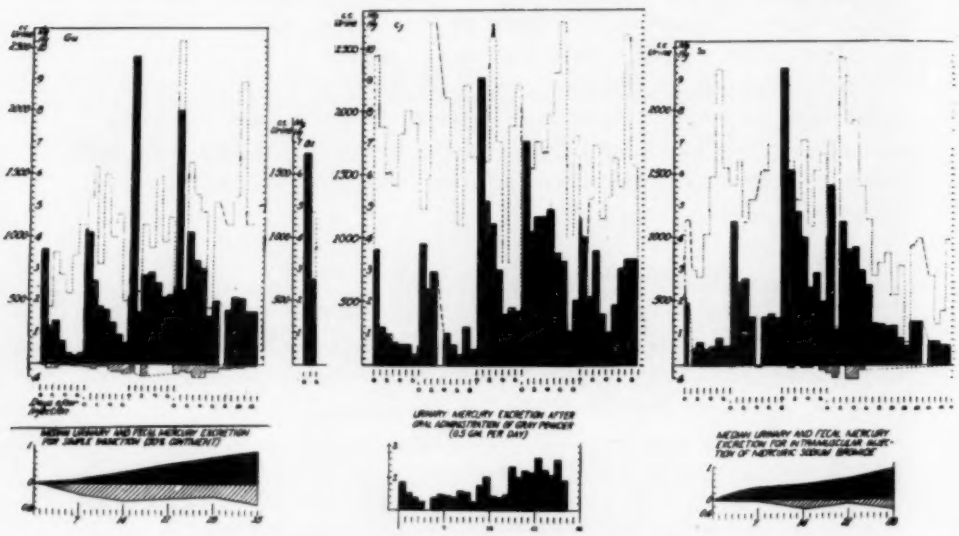


Chart 2.—Total daily urinary and fecal excretion of mercury and volume of urine following weekly intramuscular injection of mercuric salicylate (1 cc. = 60 mg. of mercury). The heavy black indicates metallic mercury plotted 0.2 mg. to the spaces of the ordinate. The dotted line indicates amount of urine in cubic centimeters. The striated portion below the abscissa denotes feces in terms of 0.2 mg. to the spaces of the ordinate running below the abscissa. Cribbed areas above the heavy black indicate what the total amount of mercury for that day would have been if it were for twenty-four hours instead of a fraction of twenty-four hours. Areas in which no specimen was collected are indicated by a line across the space. The three lower charts show for comparison the median urinary and fecal excretion of mercury on the same scale for simple inunction (50 per cent ointment); for injections of mercuric sodium bromide, and for oral administration of mercury and chalk.

progress. It may be that this is the portion of the mercuric salicylate with the therapeutic action. Its quantity would seem sufficient for this purpose, for, as is shown in chart 2, the continuous excretion of salicylate exceeds that following injections of mercuric bibromide.

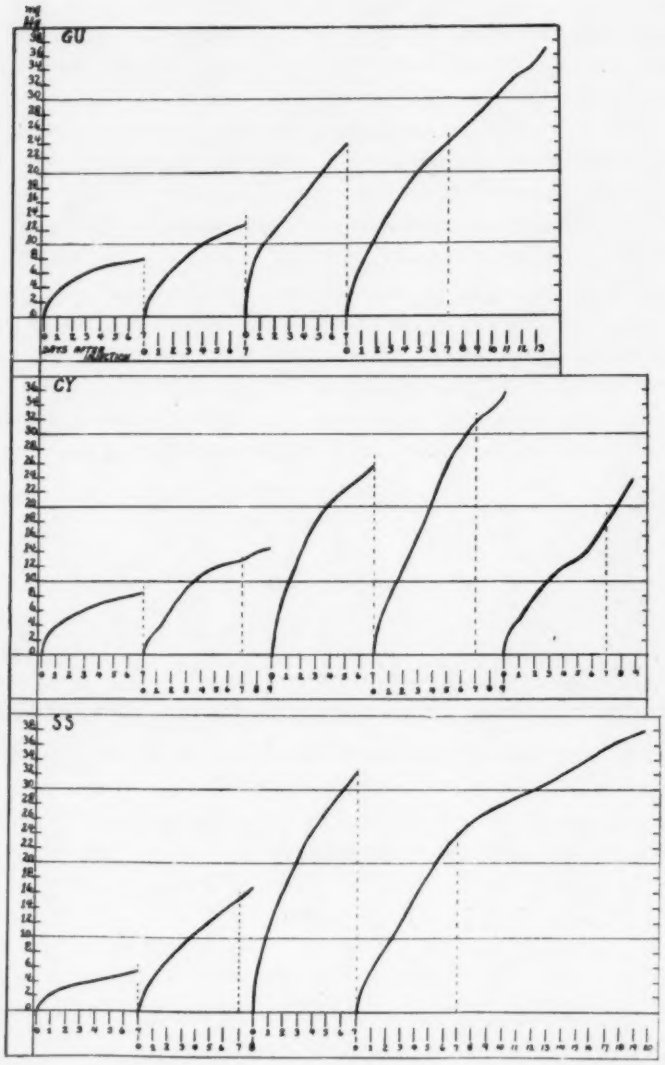


Chart 3.—Cumulative excretion of urinary mercury following weekly intramuscular injection of mercuric salicylate. Each curve indicates the excretion of mercury over a period of seven days, or as in the case of C. Y. with the second injection, over a period of nine days. Each new injection begins at the base line. Note that with G. U. the fourth injection at the end of seven days reaches only the level of the third injection; that the fourth injection with C. Y. is still higher than the third injection, but that with the fifth injection there is a definite decrease in the height of the excretion; with S. S. there is a decrease in the excretion after the third injection.

DAILY OUTPUT OF URINE

As may be seen from charts 1 and 2, each of the first three injections was followed by an increase in the urinary output, which reached a maximum on the day of injection, or sometimes one or two days later. This diuresis increased progressively following the first three injections and then declined. As observed in patient C. Y., the maximum for twenty-four hours attained on any one day was: 2,420 cc. after the first injection, 2,700 cc. after the second injection, 3,200 cc. after the third injection and 2,700 cc. after the fourth injection.

In view of our meager statistics, it would appear that mercuric salicylate is at first diuretic, perhaps to be explained as a slight irritation of the renal epithelium. After continued use there is, perhaps, sufficient irritation of the kidneys to result in a mild nephrosis and a lessened excretion. This action can probably be interpreted as analogous to the diuresis from mild mercurous chloride and merbaphen (novasurol).

	Urinary Mercury	Fecal Mercury	U:F
6-7 days after the first injection	0.30	0.16	1.9
0-1 day after the second injection	4.12	0.18	23.
6-7 days after the second injection	0.64	0.32	2.
0-1 day after the third injection	9.66	0.30	32.2
2-3 days after the third injection	2.78	0.39	7.1
5-6 days after the fourth injection	1.46	0.24	6.1

Lomholt felt that no absolute relation existed between the mercuric content of the urine and the urinary output. He stated that he had noticed both polyuria and oliguria while using mercurial preparations. Nevertheless, he was rather inclined to the belief that the excretion of a large amount of mercury is generally accompanied by a corresponding diuresis. This is our experience.

FECAL EXCRETION

Our data concerning fecal excretion are meager, since the feces were collected throughout the whole treatment for only one patient, G. U. The feces of another patient, S. S., were collected after the third and fourth injections. In both cases, the fecal mercury attained a maximum of 0.4 mg. per day, and in patient G. U. it remained at this level for some time. The fecal excretion is therefore much less than the urinary. The fecal fluctuations are relatively small; consequently the urinary-fecal ratio of mercury depends chiefly on the level of the urinary excretion. This is high immediately after the injection, thus giving a high urinary-fecal ratio; then as the urinary excretion declines, the urinary-fecal ratio also decreases. As a typical example, the ratio for G. U., is in the table.

One must therefore conclude that the urinary proportion of excreted mercuric salicylate may rise to over thirty times higher than the fecal, but the fecal excretion may at times reach the ratio of 1:2. During the thirty-four days of the experiment, the total excretion of mercury amounted to 82.27 mg. in the urine and 7.05 mg. in the feces, so that the average urinary-fecal ratio (U:F) was 11.7.

PROPORTION OF MERCURY EXCRETED AND RETAINED

A direct and absolute measurement of the total excretion and retention of mercury was made only in the patient whose feces were collected continuously. For the other patients we have definite figures only for the urinary excretion. These, however, permit a fair approximation of the total excretion and retention, since with the salicylate only a minor part of the total excretion of mercury occurs in the feces; in our patient G. U., the total amount excreted in feces was only about one twelfth of that excreted in the urine. In Lomholt's patient with the highest excretion, one fourth of the excretion of mercury was found in the feces; but even this ratio would not alter the general conclusions deduced from the urine. Our results may be illustrated by the balance of mercury two days after and a week after the first administration, and at the end of the whole course.

At the end of two days (or more exactly, forty-two hours in most cases) after the first injection of 0.1 Gm. of the salicylate, corresponding to 60 mg. of mercury, there had been excreted in the urine of the four patients 2.78, 4.39 (U+F=4.62), 4.77 and 9.28 (U+F=9.34) mg. of mercury, equivalent to 4.63, 7.32 (U+F=7.7), 7.96 and 15.47 (U+F=15.57) per cent of the injected mercury; between 85 and 95 per cent of the mercury was retained.

At the end of the week after the first injection, there had been excreted in the urine of the three patients 5.62, 7.96 (U+F=8.63) and 8.34 mg. of mercury, equivalent to 9.37, 13.27 (U+F=14.4) and 13.9 per cent of the injected mercury; between 85 and 90 per cent was retained.

At the end of the whole course, patient G. U. had received four injections at intervals of a week, with an after-period of two weeks. Therefore, a total of 240 mg. of mercury was injected, and the collection period comprised thirty-four days. The total recovered in the urine was 82.3 mg.=34 per cent; in the urine and feces together, 89.3 mg.=37.2 per cent of the amount injected.

Patient S. S. was treated in the same manner, except that the after-period extended for three weeks, or to the forty-second day. The total excretion in the urine was 92.6 mg. of mercury or 38.6 per cent of the amount injected.

Patient C. Y. received five injections, at weekly intervals, and there was an after-period of nine days. The total collection period therefore comprised forty-one days; the total mercury administered was 300 mg.; the total excretion in the urine was 108.3 mg. or 36.1 per cent of the amount injected.

At the end of the course of four or five injections and after-period of one or two weeks, the total urinary excretion in the three patients was therefore 82.3 (U+F=89.3), 92.6 and 108.3 mg. of mercury, equivalent to 34 (U+F=37.2) 36.1 and 38.6 per cent of the amount injected. The total excretion in the course may therefore be adjudged as about four-tenths of the amount injected, leaving about six-tenths retained; with four injections of 0.1 Gm. of salicylate, the retention at the end of the course amounts to about 150 mg. of mercury and with five injections, to nearly 200 mg. These figures, both the absolute amounts excreted and retained, are considerably higher than those for the other methods of administration that we have so far studied.[19] During four weeks of inunctions of 50 per cent mercurial ointment, the total amount of excretion averaged 24 mg., that is, about one fourth of that with the injections of salicylate; during four weeks of daily injections of 10 mg. of mercury bibromide (=5.5 mg. of mercury), the total excretion averaged 20.5 mg., also about one fourth of that with salicylate; the total retention of mercury averaged 130 mg., or almost as much as the retention under the treatment with salicylate.

Our figures for the urinary excretion of mercury after injections of salicylate harmonize well with those of Lomholt, but his data for the feces are rather higher than ours. He injected the equivalent of 154 and 176 mg. of metallic mercury into two patients during the course of twenty-two and thirty days. During this time, 38.6 and 49.4 per cent were excreted, and of this 74.5 and 81.2 per cent, respectively, in the urine, and 25.5 and 18.8 per cent in the feces. He stated the belief that this rapid excretion is not found with any other preparation—certainly not with an insoluble one. He ascribed it to the peculiar chemical formula of mercuric salicylate.

COMMENT

In view of our observations, it appears doubtful whether in the treatment of patients with syphilis, mercuric salicylate should be administered oftener than once in seven days. The drug is excreted rapidly, it is true, but even after the high preliminary excretion of

19. Cole, H. N.; Gammell, John A.; Rauschkolb, J. E.; Schreiber, Nora, and Sollmann, Torald: The Clinical Excretion of Mercury II. After Intramuscular Injections of Mercuric Bromide and Simple and Clean Inunction, Arch. Dermat. & Syph. **17**:625 (May) 1928.

mercury following an injection, sufficient mercury is still excreted to surpass the mercury excreted after simple inunctions, injections of mercuric bibromide or mercury with chalk by mouth. Moreover, we fear that if the drug is given too often, too large a dose of mercury may be forced on the kidneys at one time, with danger of an acute inflammation. Even with the doses used once a week, after from three to four injections, one notes phenomena which may be interpreted as signs of a mild nephrosis, in the form of increased urinary output and progressive increased excretion of mercury, followed by lowered output of urine and lessened excretion of mercury as the effects of the nephrosis increase. In view of our observation of such large mercuric excretion as compared with that of simple inunction, mercuric bibromide and mercury with chalk, the question may be asked whether the therapeutic effects of mercuric salicylate are correspondingly superior. At this time, we are unwilling to answer this question unequivocally. The value of mercury inunctions, and of injections of mercuric bibromide or iodide in the treatment of patients with syphilis may be considered established; and possibly Lomholt's contention is correct, that a portion of the mercury of mercuric salicylate is excreted in an inactive form. Yet, in view of our observations, we feel that mercuric salicylate is not to be ignored when one considers its safety from a clinical standpoint, its ability to produce signs of mercurialization in the patient, its high cumulative mercuric excretion and its definite therapeutic action on syphilitic lesions.

CONCLUSIONS

The excretion of mercury was studied quantitatively on patients receiving intramuscular injections of an oil suspension of mercuric salicylate. The data led to the following conclusions:

The rate of the urinary excretion of mercury is high for the first two to four hours after the injection; it then falls rapidly to a much lower level. The salicylate therefore behaves at first as a soluble, and later as a relatively insoluble preparation. Because of the short duration of the period of rapid excretion, only a small fraction of the mercury is eliminated in this form, the total excretion in the first two days being only from 5 to 15 per cent of the amount injected; at the end of a week, from 85 to 90 per cent of the mercury is still unexcreted. This represents an accumulation of depots of mercury for the continuous absorption and excretion of mercury, which take place for long periods at a somewhat higher level than with inunction or with intramuscular injections of the usual doses of mercuric bibromide. The total retention of mercury, one or two weeks after the termination of the course of four or five injections of the salicylate at weekly intervals, corresponds to more than half of the amount injected, and may attain 150 mg. of mercury. It, therefore, appears

unnecessary to us to inject mercuric salicylate oftener than once a week; more frequent administration would be inadvisable, partly for fear of excessive accumulation and partly also because there are indications of renal irritation.

The salicylate produces a diuretic response, and the permeability to mercury increases progressively for the first two or three injections, and then suffers a definite decline.

The fecal excretion of mercury in the one patient in whom it was followed through the whole course, amounted to about one twelfth of the urinary excretion; a similar relation was observed in another patient during the period when it was studied.

Abstracts from Current Literature

Treatment of Tabes and Cerebral Syphilis with Malaria. Franklin G. Ebaugh, J. A. M. A. **91**:1020 (Oct. 6) 1928.

This study was made on nine patients with cerebral syphilis and fifteen with tabes. They were all selected cases without evidence of cardiac or renal involvement. They have been followed up from periods of six months to three years. The nine patients with cerebral syphilis had all received the usual antisyphilitic treatment before they were treated with malaria. They had from six to fourteen paroxysms. The clinical improvement in eight of the nine was so pronounced that the use of malaria is indicated in all such cases, especially those in which the patients do not respond to treatment by older methods.

Similar results were obtained in patients with tabes. Lightening pains especially were greatly relieved. The author is conservative in his estimates of the use of malaria but definitely believes that it should be used when subjective complaints are not improved with older methods of treatment.

Symptoms, Diagnosis and Pathology of Tularemia. Edward Francis, J. A. M. A. **91**:1155 (Oct. 20) 1928.

From a study of 679 case reports, Francis takes up the subject in typical textbook manner. Of the four clinical types the ulceroglandular was the most common, then the oculoglandular, glandular and typhoid types in the order named. The symptoms, diagnosis and pathologic conditions are discussed fully. In thirty-two of the cases definite skin eruptions, other than the "typical" skin manifestations of tularemia, were noted. These varied from a few isolated hemorrhagic macules to large blotches of toxic erythema. The majority were erythematous papules or papulopustules. Subjective symptoms were mild or absent. Two patients developed florid acne, one jaundice and one herpes. Distribution was generalized, the majority showing involvement of the face, neck, chest and back.

Phagedenic Destruction of the Male Genitalia. John H. Labadie, J. A. M. A. **91**:1447 (Nov. 10) 1928.

Seven cases are reported of phagedena of the genitals. In this condition, painful destructive ulcers beginning in chancres or chancroidal infections spread by direct extension. Untimely surgical intervention as circumcisions or dorsal slits, with the introduction into the deeper tissues of saprophytic organisms, are the chief etiologic factors. The microscopic picture is that of a chronic inflammatory ulceration. The lesions have proved most refractory to treatment. The author calls attention to the fact that little is to be found of this condition in the literature. The report in *The Journal of the American Medical Association* is an abbreviation of the original article.

Hereditary Dystrophy of the Nails. Harold B. Thompson, J. A. M. A. **91**:1547 (Nov. 17) 1928.

This patient was of the fourth generation in a family affected with dystrophy of the nails. Her father, grandfather and great-grandfather had been similarly affected. Response to roentgen therapy was slightly encouraging. The report is of interest as an example of mendelian transmission of characteristics. A diagram of the family tree is included.

HODGKIN'S DISEASE THIRTEEN YEARS AFTER TREATMENT WITH ROENTGEN RAY AND RADIUM. G. ALLEN ROBINSON, J. A. M. A. **91**:1548 (Nov. 17) 1928.

This patient had received roentgen and radium therapy from time to time over a period of thirteen years. Radiation tended definitely to reduce tumor masses, relieve pain, and perhaps prolong life.

RATTNER, Chicago.

PAINFUL NODULE OF THE EAR. W. DUBREUILH and DE GURBERT, Ann. de dermat. et syph. **9**:729 (Sept.) 1928.

The authors add six cases of this disorder to the twenty-four already recorded in the literature. Their cases did not differ in any way from those previously described. The condition, unless treatment is given, endures indefinitely. The authors believe that excision with suture is the best treatment. Even this measure is sometimes followed by recurrence on the periphery, as happened in one of their cases.

HUTCHINSONIAN TEETH: ASSOCIATION AND PATHOGENESIS. C. AUDRY, Ann. de dermat. et syph. **9**:737 (Sept.) 1928.

Audry states that hutchinsonian teeth are a fairly common manifestation of congenital syphilis, more frequent than labyrinthitis, and at least as common as interstitial keratitis.

Hutchinsonian teeth, practically speaking, occur only in cases of congenital syphilis; strictly speaking, they may appear in other disorders. The author says that Hutchinson's triad is exceptionally rare. He has only seen it in three cases. Dental deformities frequently occur with hutchinsonian teeth. A case is described in which the latter was associated with ogival palate and irregular implantation of the teeth.

Notched incisors are the result of faulty development in the superior mandibular buds. The determination of the defect occurs early, probably before the fifth week of fetal life. Embryologic study is the key to this problem.

A TYPICAL TRICHOPHYTOSIS OF THE GLABROUS SKIN CAUSED BY T. VIOLACEUM. G. MGUEBROW, Ann. de dermat. et syph. **9**:742 (Sept.) 1928.

The author describes and illustrates ten cases (and has seen fourteen more) in each of which he has found the organism mentioned in the title. Speaking broadly, the lesions were erythematosquamous in type and pruritus was practically absent. They endured a long time, and in nearly all cases invasion of the scalp and nails was present. Morphologically, psoriasis or chronic eczema was most closely simulated. The differentiation from these and other erythematosquamous diseases is given at great length. *T. violaceum* is found in the scales; therefore, the disorder is not a trichophytid. Cure is obtained only with difficulty. Chrysarobin and sulphur ointment gave the best results in the glabrous lesions; weak tincture of iodine and potassium permanganate baths are recommended for plantar and palmar invasion.

GENERALITIES CONCERNING FUNGUS DISEASES OF THE SKIN. II. MEMOIR: TRICHOPHYTON VIOLACEUM. R. SABOURAUD, Ann. de dermat. et syph. **9**:769 (Sept.) 1928.

In his first memoir, Sabouraud considered favus. In this he discusses infection with *T. violaceum*, because this organism seems to be widespread geographically and responsible for more cases than any other fungus of like order. It is uncommon in France; but was one of the first fungi to be described by the author in 1892-1895.

Microscopically, it is a true endothrix. A hair invaded by this parasite becomes fragile, so that when the scalp is involved the hairs are broken off practically at

the cutaneous surface, and the "black dot" clinical type is produced. Tinea capitis caused by this organism may persist into adult life; all of Sabouraud's cases in the adult have been due to this organism. This explains the many cases of adult tinea capitis reported in Russia where *T. violaceum* is a common organism. The author has rarely encountered this fungus in the beard, but it is said to be fairly common in this locality in other countries. Again, its invasion of the nails is rarely observed in France, though frequent in other Mediterranean countries. Recently, Russian authors have described extensive, figured and marginate patches produced by this parasite. Again, cases of deep abscess formation, lymphatic and even osseous invasion have been ascribed to this organism.

Sabouraud studied a culture of *Achorion violaceum* sent him by Bruno Bloch (who first isolated that *Achorion*) and concluded that it was doubtful that Bloch's organism was a true *Achorion*.

T. violaceum has many peculiarities and features sharply differentiating it from other *Trichophytons*, so much so that Sabouraud thinks it might be justifiable to take it out of the *Trichophyton* group and designate it *Erythrophyton*.

MICHAEL, Houston, Texas.

DERMATOLOGIC ABSTRACTS

THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION

SCLERODERMA AND CALCINOSIS. R. H. DURHAM, Arch. Int. Med. **42**:467 (Oct.) 1928.

Fourteen cases of calcinosis associated with scleroderma or sclerodactylia have been collected by Durham and added to the nine cases reported in 1911. In four of the eight cases of scleroderma and calcinosis, there was an accompanying sclerodactylia. In three cases of sclerodactylia with calcinosis, there was no recognizable scleroderma. That the combination of scleroderma and calcinosis constitutes a distinct pathologic entity, despite the infrequent occurrence, is suggested by the usual location of the calcinosis, by the fairly characteristic type of deposit and by the close local relationship of the two conditions (deposits usually in areas of scleroderma). It is nowise clear whether calcinosis with scleroderma results from local metabolic alterations or deranged inorganic metabolism. As in other types of pathologic calcification, the colloidal proteins are thought to play a prominent rôle.

PREVALENCE OF SYPHILIS AND GONORRHEA IN NEW YORK STATE. A. PFEIFFER and H. W. CUMMINGS, Michigan State J. Med. **28**:1147 (Oct. 1) 1928.

The total population of the territory covered in the survey reported on by Pfeiffer and Cummings was almost 6,000,000. The prevalence rates for males were about the same for syphilis (3.34) and gonorrhea (3.00), whereas for females the syphilis rate (1.93) was more than twice the gonorrhea rate (0.88). Of the women who were under treatment for syphilis on the day of the survey, 44 per cent were attending clinics — more than double the corresponding proportion (21 per cent) under treatment for gonorrhea. The data available do not warrant definite conclusions regarding the prevalence of syphilis and gonorrhea according to the urban or rural character of the population or according to the density of population. They have given a basis, imperfect perhaps, but of real value, for estimating the relative prevalence of syphilis and gonorrhea. The survey has given for the first time information on which even a rough estimate of the incidence of gonorrhea could be based. It has proved strikingly that the general practitioner in New York state is treating syphilis and gonorrhea. It shows that the ten years of organized effort by the federal government and the state division of social hygiene has probably resulted in getting thousands of infected persons under scientific treatment. It has demonstrated that these diseases are sufficiently prevalent to constitute a major problem in preventive medicine.

RELATIVE LOW HUMIDITY OF ATMOSPHERE AND MUCH SUNSHINE, AS CAUSAL FACTOR FOR GREAT PREVALENCE OF SKIN CANCER IN AUSTRALIA. H. LAWRENCE, M. J. AUSTRALIA **2**:403 (Sept. 29) 1928.

Skin cancer is said to be a very prevalent disease in Australia and is, relatively speaking, more common in Australia than in England or European countries. Lawrence's experience has been that the number of cases coming under the heading of the epithelial triad (keratosis, rodent ulcer and epitheliomas) certainly suggests that this condition of skin cancer is quite a serious matter in Australia. The percentages of incidence are: rodent ulcer, 6.82; keratosis, 4.38, and epitheliomas, 1.975, or a total percentage of 13.23. Lawrence, with others, feels that the relatively low humidity of the atmosphere in Australia probably favors the irritating effects of the solar rays in the production of keratoses, rodent ulcer and epithelioma. The humidity of the atmosphere of Australia is as low as 30, 40, 50 and 60 per cent for the greater portion of the continent and remains so for a large part of the year.

THYROID TREATMENT OF FACIAL EDEMA. E. APERT and BACH, Arch. de méd. d. enf. **31**:611 (Oct.) 1928.

A case of facial and palpebral edema in a girl, aged 3, without any signs or symptoms of renal disease, is reported by Apert and Bach; the edema disappeared each time that thyroid treatment was begun but always reappeared shortly after the treatment was stopped.

DIATHERMY IN LUPUS. H. BORDIER, Rev. gén. de clin. et de thérap. **42**:641 (Oct. 6) 1928.

Bordier describes two cases of lupus vulgaris in which the patients had been treated for years without success by various methods: both were cured in a short time with electrocoagulation. The author believes that electrocoagulation is the best form of treatment for the majority of cases of lupus vulgaris. One reason for the superiority of this treatment is the fact that the high temperature not only produces a change in the tissues in which the tuberculous lesion has developed but also destroys the tubercle bacilli. Another good feature of this form of treatment is the fact that the resulting scars are supple.

CHICKENPOX IMMUNIZATION. K. VON KÉSMÁRSZKY, Arch. f. Kinderh. **85**:1 (Aug. 31) 1928.

In fifty of fifty-one cases Késmárszky produced immunity against chickenpox by intracutaneous injection of 0.1 cc. of citrated blood from a patient with chickenpox. The blood was withdrawn within thirty-six hours of the appearance of the disease. There was no local or general reaction worth mentioning, and undesirable results were not manifest. The length of the period of immunity is not known.

CAUSES AND TREATMENT OF ALOPECIA. R. HABERMANN, Deutsche med. Wchnschr. **54**:1560 (Sept. 14) 1928.

In a large number of animals of various kinds, Habermann found that a preparation of cholesterol was more effective in promoting the growth of hair than petrolatum, with or without cholesterol, or dry massage. Pure alcohol seemed in some cases to check hair growth. Loss of hair from thallium poisoning could be prevented by the cholesterol preparation. It was applied with a soft brush. The effects of the treatment in thirty-five patients with alopecia seborrhoica were highly favorable. The subjective symptoms disappeared, the production of scales and of sebum on the scalp diminished. In most cases there was also increased growth of hair. In some cases a distinct increase in the cholesterol content of the hair could be determined. In hair that was starting to turn gray, the amount of pigment was increased.

PSYCHOGENIC ORIGIN OF HERPES LABIALIS. R. HEILIG and H. HOFF, Med. Klin. **24**:1472 (Sept. 21) 1928.

Heilig and Hoff selected three women, two with a compulsive neurosis and one with psychopathic depression, who were used to having herpes appear on the lip after an unpleasant emotional experience. By animal experimentation it was determined that they had herpes virus in the nasopharynx. In hypnosis the patients were made to repeat an unpleasant emotional experience and at the same time the occurrence of herpes was suggested to them. In each of these cases the herpes appeared within forty-eight hours. Hypnotic suggestion alone failed to induce the herpes. The authors determined the opsonic index for staphylococcus and for *Bacillus coli* in the normal state and two or three hours after the emotional experience undergone during hypnosis. In all the cases there was a distinct reduction in the opsonins after the emotional experience. They conclude that the natural defense of the organism to infection is lowered by unpleasant emotional experiences.

TREATMENT OF ANGIOMAS. A. HUSTON, Scalpel **81**:873 (Aug. 4) 1928.

For the treatment of large angiomas of the face, Hustin recommends several injections of 10 cc. each of a 100:100 solution of sodium citrate. These injections are repeated every eight or ten days until the tumor has entirely disappeared. Using this method the author completely obliterated an angioma the size of a walnut, located at the level of the labial commissure, in a young woman. Eight injections separated by a five or six day interval sufficed. Before making the injection one should convince oneself that the point of the needle is indeed in the lumen of a vessel, because the injection of the concentrated solution of sodium citrate into the tissues would be painful and might result in an eschar. Instead of sodium citrate, sodium carbonate, sodium salicylate, red mercuric iodide, or one of the quinine salts may be used. The author believes that the quinine salts are most suitable because they do not produce a very extensive eschar if unintentionally injected outside the vessels. The advantages of the method are that the injections are painless, are nontoxic, and produce little reaction. The tumor retrogresses gradually and does not leave a scar, unsightly projection or depression.

RADIUM IRRADIATION OF CANCER OF THE SKIN. F. DAUTWITZ, Strahlentherapie. **29**:634 (Aug. 15) 1928.

One hundred and eighty-six cases of skin cancer treated with radium are reported by Dautwitz. One hundred and eight of the patients had previously received no treatment other than that with ointments or with the caustic pencil; the remaining seventy-eight had had surgical, roentgen or radium treatment without satisfactory results. The lesions were on the face in all except nineteen cases. In four they were on the trunk, in eleven on the extremities and in three on the hairy part of the head. In thirty-four cases lymph glands were involved. External irradiation was given with the aid of a plate apparatus of Dautwitz's design. He uses chiefly the β rays, even in superficial ulcer processes. He does not agree that, in proper doses, the β rays act as a pure caustic, destroying both diseased and healthy tissue. He obtained cosmetically faultless scars by their use. He has not found any untreated ulcerated skin cancer that refused to respond to β rays. In his opinion one should not speak of insensitivity to radium in general, but only of insensitivity to the γ rays. The success of radium treatment in many skin cancers seems to depend on whether merely electromagnetic rays or chiefly corpuscular rays reach the lesion. He gives from two to eight treatments with fractioned doses, the duration of each being from four to eight hours, with intervals of from twelve to thirty-six hours. In the group of previously untreated patients there were 70.4 per cent of cures lasting over three years, and 29.8 per cent of cures lasting from five to fifteen years. In the group of patients previously treated by irradiation or surgery, there were 50 per cent of cures lasting three years and 19.2 of cures lasting from five to fourteen years. He reports in brief fourteen cases and gives twenty-nine pictures showing the condition before and after treatment. An extensive bibliography accompanies the article.

ROENTGEN THERAPY OF TUBERCULOUS ADENITIS. A. EGHIAYAN and E. WYSS, Rev. med. de la Suisse Rom. **48**:721 (Sept. 10) 1928.

According to Eghiayan and Wyss, the results of roentgen therapy of peripheral tuberculous adenitis differ according to the type treated: 1. In simple hyperplasias of the glands the results following exclusive roentgen therapy are excellent. 2. In the suppurative, caseous forms of adenitis, roentgen therapy alone usually does not suffice. The resorption of pus or of caseous masses is not impossible, particularly if the glands lie deep; however, a great deal of time would be required for this. Most frequently the suppuration finally reaches the surface and passes through the thinned skin. From esthetic considerations this spontaneous evacuation should be hastened by a minor surgical intervention. 3. In the ulcerative, fistulous forms roentgen therapy alone suffices in favorable and recent cases. The authors give the following incontestable advantages of roentgen therapy over total extirpation in cases of peripheral tuberculous adenitis: 1. It is bloodless, is painless and does not necessitate anesthesia; for all these reasons it is less feared by the patient. 2. Local recurrences, which play such an important rôle in patients treated surgically, are much less frequent after roentgen therapy. 3. In the cases in which the lesions are very extensive or deeply situated, as well as in the cases of multiple ulcerations, surgery is frequently of no value, whereas roentgen therapy gives rapid results. 4. The esthetic results are much better with roentgen therapy correctly used; this problem is of great importance socially, particularly in the cases of cervical foci in women. In the cases of simple hyperplastic adenitis, roentgen therapy leaves no scar whatever; in the suppurative and fistulous forms, even when it is necessary to associate minor surgery with the roentgen therapy, the esthetic results with roentgen therapy are incomparably better than those with surgical treatment alone, which leaves marked, occasionally keloid scars. 5. Total extirpation is accompanied by certain dangers which cannot always be avoided even with an irreproachable technic: section of facial, hypoglossal, spinal accessory, and cervical sympathetic nerves and persistent lymphatic edema of the corresponding arm or half of the face.

RADIOTHERAPY OF CANCER OF EYELID. S. DE VRIES, Nederl. Tijdschr. v. Geneesk. **73**:3904 (Aug. 11) 1928.

Of twelve patients treated with roentgen rays, only four were cured. Of the remaining eight, three were subsequently cured by radium treatment. Thirty-seven patients were treated with radium. The first of these was given a small dose to start and was not cured. Four had been "vaccinated" against radium (the cancer cells made insensitive to the rays by small doses) elsewhere. With one exception these were not cured by the later irradiation. The remaining thirty-two were treated in one sitting, the application lasting for twenty-four hours in most cases. Thirty patients were cured; in seven cases the cure has lasted from five to eleven years; in five, from three to five years; in ten, from one to three years, and in eight, from six months to one year. A prosthesis of paraffin or rubber, about 3 mm. thick, is used to protect the eyeball.

Society Transactions

NEW YORK ACADEMY OF MEDICINE, SECTION ON DERMATOLOGY AND SYPHILIS

J. J. ELLER, M.D., *Secretary*

Regular Meeting, May 1, 1928

E. R. MALONEY, M.D., *Chairman*

ANAL CHANCRE. Presented by DR. PAROUNAGIAN.

P. K., a man, a Greek, aged 31, was seen at the Bellevue Clinic for the first time on the day of presentation. He gave a history of penile chancre three years previously, for which he had been treated with twelve injections of arsphenamine. There had not been any further manifestations of the disease until two months before presentation, when a generalized roseola occurred. A hard, elevated, round lesion, the size of a dime, was detected near the anal orifice. The patient admitted sodomy three or four months previously. The glands below Poupart's ligament were markedly swollen, and there was an unusually pronounced general adenopathy. The patient indulged freely in alcohol and complained of severe headaches. The case was presented as one of possible reinfection with syphilis.

LEUKODERMA SYPHILITICUM. Presented by DR. PAROUNAGIAN.

W. W., a colored man, aged 33, was admitted to the Bellevue syphilis clinic on April 17, 1928. The results of a Wassermann test were 4 plus. He gave a history of a penile lesion fifteen years previously, which had left a conspicuous scar. He had not received any treatment. For two months, he had been unable to retract the foreskin; previous to that he had noticed a sore at the frenum. A month before admission, he had noted a papular eruption on the face and different parts of the body. He showed a marked general adenopathy and slight alopecia. The pupillary reaction was sluggish, but the other reflexes were fairly normal. He presented a marked guttate leukoderma, more or less generalized, more marked on the back, which he believed had existed for ten years.

GUMMA (?). Presented by DR. HOPKINS.

R. D., a housewife, aged 33, born in the United States, seven years before presentation had noticed a small brown growth on the left temple, which had extended gradually and had ulcerated until it destroyed the skin and soft tissues in that area. It had caused little pain. She had been treated by internal medication. The blood had never been examined.

In the left temporal region, there was a roughly circular ulcer nearly 2½ inches (6.27 cm.) in diameter, which formed a deep concave excavation which extended to the bone and invaded the scalp and outer portion of the orbit. The base was covered with red granulations which discharged a foul-smelling pus. There was a soft fungating tumor at the base; at the left lower border there was a soft tumor 1 inch (2.5 cm.) in diameter, from which pus could be expressed. There was no surrounding infiltration, or pearly thickening of the epidermis at the edge of the ulcer. The adjacent lymph nodes were not enlarged. The Wassermann test gave a reaction of 0 with alcohol and of ++++ with cholesterol; the results of the Kahn test were negative.

DISCUSSION

DR. PAROUNAGIAN: I would register a vote against the diagnosis of gumma and in favor of epithelioma. The ragged edges, and the rather hard looking border suggest a clinical diagnosis of epithelioma.

DR. BECHET: The extensive destruction of the soft parts is corroborative of epithelioma. It does not resemble a gumma. It is an unusually extensive rodent ulcer of the type that was common years ago.

DR. TRAUB: The anterior portion had a rather "punched-out" border and not the rolled edge suggestive of epithelioma of the rodent ulcer type. I think that the age of the patient is distinctly in favor of a diagnosis of tertiary syphilis. The seven years' duration should not rule out this diagnosis, because an untreated gumma so located might destroy tissue for a great length of time. Histologic examination and a therapeutic test are necessary to settle the point, but clinically, I favor the diagnosis of syphilis.

DR. CHEEVER, Boston: One point against a diagnosis of syphilis is the amount of bleeding; ordinarily with gumma there is so much deep necrosis that there is unlikely to be the amount of bleeding seen here, and there is more or less hypertrophy, which I cannot reconcile with gumma.

DR. OULMANN: I never saw a gumma of seven years' standing of such superficial character, slowly growing in size without healing or scar formation anywhere, slightly bleeding at times and with the edges as presented in this case. If a gumma were present at the beginning—which I doubt—it is now a basal cell epithelioma.

DR. ROSTENBERG: I have seen a similar case in the days before the arsphenamine era, in which the patient with an extremely large gumma on the cheek was treated with administrations of mercury and potassium iodide. This gumma finally changed to a carcinoma, and the patient finally died of a generalized carcinomatosis. I believe that this patient also had a gumma originally, but is now suffering from a carcinoma.

DR. WOLF: An interesting feature is the extent of the lesion without associated adenopathy. It is unusual for so large a lesion, if carcinoma, not to have enlarged glands in the cervical or postauricular regions, although I have seen several cases of early prickle cell carcinoma of the tongue without adenopathy. I think that a biopsy would probably settle the diagnosis. It has all the clinical characteristics of a prickle cell carcinoma.

DR. BECHET: I would like to know if the patient has received treatment.

DR. HOPKINS: The patient came to the clinic only yesterday. The differential points in the clinical diagnosis have been well brought out in the discussion. The absence of adenopathy is in favor of—not against—the diagnosis of basal cell tumor. If this were a gumma, one would expect more infiltration about it. I know of nothing but a basal cell epithelioma that could quietly destroy a quarter of the face and cause so little reaction. We have taken a biopsy, but have not yet received the report.

ACANTHOSIS NIGRICANS. Presented by DR. FEIT. (From the Service of Dr. Clark, Skin and Cancer Hospital.)

J. E., a laborer, aged 59, born in Ireland, had always enjoyed good health until two years before presentation, when he suffered from stomach trouble. He had lost about 15 pounds (6.8 Kg.). About three months before presentation, warts and brown papules began to develop on the backs of the hands and forearms, and gradually appeared on other parts of the body, as well as on the mucous membranes. As presented, there were a few large flat-topped papules on the neck and chest, the surfaces of which were somewhat verrucous. The underlying skin was a dirty brown. The palms and the lips presented a thickened, rough, corrugated appearance. Other parts affected were the axillae, the lower part of

the back, the mammillae, the oral mucosa and the foreskin. The skin had a waxy appearance and could be lifted up in folds. There was a hard, uneven, freely movable mass in the midabdomen.

Roentgen-ray examination of the stomach showed an irregularity of the outline, involving both curvatures and causing a narrowing of the pylorus. The Wassermann reaction was negative.

Histologic examination showed the characteristic phenemona of acanthosis nigricans; marked hyperkeratosis and acanthosis associated with lengthening of the papillae. There were a few pigmented cells in the papillary derma, also in the summits of some of the papillae. There was an island of degenerated connective tissue, throughout which were small blood vessels (Dr. Barthel).

DISCUSSION

DR. BECHET: It is typical of the type associated with malignancy of some internal organ. It is a replica of the case which I recently presented before this section; the patient has since died of cancer of the stomach. These two cases should make us revise our ideas of acanthosis nigricans. We are usually inclined to lay too much stress on the presence of extensive pigmentation, which I think is more common in the juvenile type. Dr. Feit's patient, as also mine, showed some pigmentation, but certainly not so extensive as we are led to expect from articles on the subject. On the other hand, in both patients the warty lesions and the velvety, papillary growth on the palms and soles and on the buccal mucosa are well marked.

DR. FEIT: Last year I had occasion to see a woman with a disease picture similar to that in this case. In my absence, she went to the Skin and Cancer Hospital and was presented by Dr. Bechet before this section. Dr. Bechet informed me that she died later of carcinoma of the stomach. The patient presented here has a pronounced pigmentation over the sacral region, the skin of which is corrugated, and there are lesions on the mucous membrane of the mouth as well as on the foreskin. The only difference in the two cases is the amount of pigmentation, which is due to the duration of the disease. In time this man will show just as much pigmentation as did the woman. This patient also has cancer of the stomach. Both patients presented hyperpigmented verrucous lesions on the skin as well as on the mucous membranes.

MULTIPLE BENIGN TUMORLIKE NEW GROWTHS (Schweninger and Buzzi). Presented by DR. FEIT. (From the Service of Dr. Clark, Skin and Cancer Hospital.)

R. W., a Russian woman, aged 49, had always enjoyed good health excepting for diphtheria fifteen years before presentation. The family history was irrelevant. The patient was a well nourished, healthy looking woman, without any pathologic changes except the condition of the skin. The eruption had started twelve years previously on the arms or neck, the patient did not remember which. Sometimes she felt a slight stinging sensation. The face, shoulders, chest and the upper part of the back and trunk were involved. First small, light gray tumors developed, which gradually involuted leaving rather sharply defined round or oval patches, the surfaces showing atrophic, depressed punctate spots, varying from the size of a pea to that of a bean, and surrounded by a slightly elevated edematous border. The tumors were pouchlike, elastic and hollow, and could be impressed like a hernia sac; they were not unlike those found in von Recklinghausen's disease. By aggregation they formed large bluish-red patches, from the size of a finger nail to that of the palm.

Histologic examination showed a thin epidermis with a rather cellular connective tissue in the corium. In the upper corium, there were dilated blood vessels surrounded by extremely edematous areas and a slight lymphocytic infiltration. There was rather marked granular degeneration of the connective tissue between

the upper third of the corium and the epidermis. This picture was typical of the clinical diagnosis. There were practically no elastic tissue fibers in the upper third of the corium. There were occasional masses of black-staining granules in the upper corium; in the lower corium and midcorium there were some coarse-staining elastic tissue fibers which appeared swollen; others were small and broken (Dr. Barthel).

DISCUSSION

DR. CHARGIN: The case presents all the features of the disease—the peculiar pitted-like atrophy, the infiltration and the distribution. An unusual feature is the size of the lesions. Neither of two cases that I have seen had such large lesions, but in other respects it seems typical.

DR. FEIT: The question as to whether these tumors should be placed among the idiopathic atrophies, the new growths or the congenital defects (Pusey) is not yet settled. They start as skin colored rubberball-like tumors which can be pressed in only to bulge out again; the older they are, the less elasticity they show. Partial involution takes place, punctate scars remaining on the surface. The development is slow, requiring in this instance twelve years to form about thirty tumors.

DERMATITIS MEDICAMENTOSA. Presented by DR. BECHET.

C. G., a white woman, aged 55, said that sixteen days before presentation she had taken a pill three times a day for two days, which her druggist reported contained codeine sulphate, acetylsalicylic acid, salicin and camphor monobromate. Three days later, the eruption had appeared; prior to its appearance the patient had never had any "skin trouble." The eruption was most extensive on the arms and neck—presenting vegetating nodules on the neck (which had subsided entirely after two or three intravenous injections of physiologic solution of sodium chloride) and ademtous, rounded, violaceous-red lesions on the arms, indistinguishable from erythema multiforme. The lesions on the arms were noticeable when presented and had not made any appreciable change after a week or so of observation. The patient apparently suffered from two distinct varieties of dermatitis medicamentosa, namely, a bromoderma on the neck from the bromine content of the monobromated camphor, and erythema multiforme-like lesions on the arms from one of the "coal tar" derivatives.

GENERALIZED SCLERODERMA. Presented by DR. FEIT. (From the Service of Dr. Clark, Skin and Cancer Hospital.)

A. G., a man, born in the United States, had had pneumonia in 1925, after which he had suffered continually from boils. None of the family had had any similar disease, and the patient gave no history of having ever taken arsenic.

The eruption had started three weeks before presentation as three rings on the anterior surface of the neck, which gradually became so stiff that he could hardly move his head in either direction. The cheeks, neck, arms and the trunk down to the pelvis were involved. The skin of the neck was glossy and hardened like parchment paper, and could not be lifted in folds; the mucous membranes were not involved. He was unable to extend his arms without pain.

Observations for arsenic in the urine showed: 160 micromilligrams per hundred grams of dried specimen—normal being 40 mg. The urinalysis showed: blood sugar, 116; chlorides, 446; urea, 13.2; uric acid, 4.16.

There was marked improvement after the patient had received three intravenous injections of sodium thiosulphate, according to the patient's own statement.

DISCUSSION

DR. OULMANN: Fourteen or fifteen years ago, I presented a boy, 4 years of age, with an acute myxedema, who presented a similar picture, besides some pigmentation. These types of acute scleroderma are due to endocrine disturbance

in the course of an intoxication, and the patient reacts well and quickly to medication with thyroid extract. My patient is in good condition and has been so for years.

DR. FEIT: The boy gives a distinct history of the lesions having started as ribbon-like bands around the neck (scleroderma en bandes). The rapid improvement after the administration of intravenous injections of sodium thiosulphate, as well as the observations of the blood chemistry (increase of the sugar and decrease of the chlorides), are all in favor of scleroderma.

A CASE FOR DIAGNOSIS (PARAPSORIASIS?). Presented by DR. ROSTENBERG.

K. W., a man, aged 56, born in this country, a painter, presented a family and previous history that were irrelevant. The trouble for which he was presented had begun about two years before presentation.

Examination showed a widespread eruption in symmetrical arrangement, involving mostly the upper extremities, chest and back—stopping at the upper half of the thighs. The individual lesions varied from yellow to rose, hardly infiltrated, slightly scaly, from 1 to 3 inches (2.5 to 7.6 cm.) in diameter, round, oval, oblong and irregular. On both elbows were larger plaques, covering the entire elbows and reaching from 3 to 4 inches (7.6 to 10.16 cm.) above and below, resembling the lesion of a fading psoriasis. The patient complained of slight itching at times.

DISCUSSION

DR. CANNON: I think that the man has too much infiltration of the lesions to call it parapsoriasis. The numerous lesions, with the amount of infiltration, speak in favor of mycosis fungoides.

DR. CHARGIN: While I cannot offer a diagnosis, I do not think it is parapsoriasis, for the reason stated by Dr. Cannon.

DR. ROSTENBERG: There is only slight infiltration which is sometimes found in parapsoriasis. So far, to my mind, it is a picture of parapsoriasis in plaques, but I will take a biopsy and present the patient again later.

NEVUS LINEARIS. Presented by DR. RULISON.

A white girl, aged 19 years, was admitted to the Skin Department of the Cornell Clinic on April 30, 1928, with an eruption that had started at 3 months of age as a red macule on the buttock. Soon afterward similar red lesions appeared on the toes and fingers of the left side. The lesions later became elevated, warty and grayish, and similar lesions appeared on the left buttock and the hands and feet. One month prior to presentation, the same type of lesion appeared on both sides of the chest. There were elevated, verrucous, linear lesions symmetrically placed on both buttocks and hands, the flexor surfaces of the wrist and feet and on the sides of the chest.

TERTIARY SYPHILIS (GUMMA). Presented by DR. CANNON.

J. S., aged 39, a salesman, born in the United States, was first seen in the Vanderbilt Clinic on April 19, 1928, because of an ulceration on the upper lip and nose. There was a definite history of inadequately treated early syphilis. About a year previous to presentation, an indurated swelling appeared on the side of the nose, and since then it had gradually spread, involving most of the nose and upper lip.

A great deal of the cartilaginous portion of the nose had been destroyed, leaving a serpiginous, raised border which showed papillomatous excrescences in places. The condition extended down on the upper lip, forming a semicircle from the right part of the lip over the dorsum of the nose to the left part of the lip. There was some scar formation around the external nasal orifices. The uvula was abnormally white and did not appear to have its normal elasticity. The Wassermann reaction was 4 plus, and the results of the Kahn test were 6 plus.

FOX-FORDYCE DISEASE. Presented by DR. GROSS.

A. V., a white woman, aged 21, a machine operator, born in the United States, said that the eruption had begun, about a year before presentation, with itching and that later the skin had become slightly thickened and covered with "pimples."

In both axillae there was an erythematous, grayish-brown discoloration of the skin which was studded with numerous follicular papules and areas of moderate lichenification of the skin. There was some excoriation due to scratching. There was a decreased amount of hair. A similar but less extensive eruption was present on both breasts and in the pubic region.

A biopsy had been taken but not yet reported.

DISCUSSION

DR. TRAUB: The lesions in the axillae, with the typical lichen-like papules, loss of hair, etc., are characteristic of Fox-Fordyce disease. The scratched papules or papulovesicles on the breasts far away from the areola about the nipples, on the other hand, are not a part of this syndrome and should not be mistaken for such just because of the pruritus.

ACRODERMATIS CHRONICA ATROPHICANS. Presented by DR. GROSS.

M. B., a woman, aged 56, a house-worker, born in Ireland, was first seen in the Vanderbilt Clinic on April 20, 1928. The duration of the eruption was thirteen years. A year after a serious illness, at which time the legs were swollen, she first noticed a diffuse reddish discoloration of the skin, which had persisted up to the time of presentation.

Both legs and thighs up to the hips were involved with a diffuse condition, which gave the extremities a cyanotic appearance. On close examination, with the exception of a few small areas, the skin showed a paper-like atrophy, which was most marked around the knees. Varicose veins were seen through the atrophic skin and even the finest venous nets were visible in certain parts. On the hips and upper parts of the thighs was a marked erythema and brownish discoloration combined with marked atrophy of the skin. Around the elbows there was a similar condition, the periphery of which was slightly erythematous, while toward the center the tissues appeared slightly infiltrated and the skin more atrophic. The Wassermann reaction was negative.

LICHEN NITIDUS. Presented by DR. MALONEY.

E. P., a colored girl, aged 8, born in the United States, presented an eruption on the forehead, neck, elbows, chest, abdomen and the upper parts of both thighs. This eruption consisted of minute colorless, shiny, more or less rounded, flat papules from the size of a pinpoint to that of a pinhead. These papules were discrete, but were arranged more or less in groups or patches. The eruption was of one year's duration, and had started on the back and spread gradually to the other parts involved.

The histologic examination of one of the papules showed the picture of lichen nitidus.

PITYRIASIS ROSEA. Presented by DR. SPIEGEL.

This patient had been presented at the last meeting of the section. The eruption disappeared in three weeks. The biopsy report was: The process was a generalized edema of the epidermis, papillary body and corium, but most marked in the first two. The other changes in the epidermis were parakeratosis and disorganization. The process was obviously pityriasis rosea or exudative erythema, and the presence of hemorrhage slightly favored the latter view, while the scaling slightly favored the former. There was no remote suggestion of lichen planus or any other condition besides the two mentioned.

PHILADELPHIA DERMATOLOGICAL SOCIETY

Meeting May 4, 1928

CARROLL S. WRIGHT, M.D., *Secretary*

LUPUS VULGARIS (PSORIASIFORM). Presented by DR. CHAMBERS.

The patient, aged 50, a native of Germany, who had been in this country for seventeen years, complained of an eruption of forty-five years' duration. Nodular lesions were located on the chin and in the left cubital region. The biopsy showed a typical tuberculosis; the results of guinea-pig inoculation have not been reported.

DISCUSSION

DR. WEIDMAN: I agree with the diagnosis. I saw the sections—classic tuberculosis with necrosis in the center of the granulomatous infiltrations. Clinically, the lesions at the bend of the elbow show a large amount of scaling, and if it were not for the telltale translucent nodule-like lupus tumidus on the periphery, one might think this was one of those cases of lupus vulgaris erythematoides of Leloir in a rather unusual position. The lesion on the chin might cause a great deal more difficulty in making a diagnosis. This illustrates well the extreme slowness with which these lesions develop; the man says the disease began when he was 5 years of age.

A CASE FOR DIAGNOSIS. Presented by DR. RAPP for DR. SCHAMBERG.

C. S., aged 73, was presented two months previously because of a condition which still persisted. It consisted of marginated patches showing considerable pustulation, vesiculation, scaling and crusting, which were present on the hands and feet. He had received extensive treatment, including roentgen-ray and ultraviolet light therapy. We have tried to get cultures on three occasions, on two of which the cultures were sterile; once a culture of *Staphylococcus albus* was obtained. The patient was also given autogenous vaccine, but was not benefited by it.

DISCUSSION

DR. WRIGHT: I think the condition in this case corresponds to that in a case described by Dr. James Herbert Mitchell of Chicago at a recent meeting of the American Dermatological Association. He described these cases in which the clinical appearance would warrant a diagnosis of epidermophytosis, and yet, fungus would not be demonstrable on repeated cultures and on microscopic examinations. Dr. Mitchell did not attempt to classify these cases under a different heading. He reported the observation of staphylococci and other organisms in the pus, but he did not know whether this was a causal agent or just an associated observation. I think we all see these cases now and then. If treatment were based on a clinical appearance alone, one would immediately use Whitfield's ointment with perhaps potassium permanganate baths. However, when a microscopic examination is made, the fungus cannot be demonstrated. Perhaps Dr. Weidman can tell us a little more about this.

DR. WEIDMAN: Was material taken from the hands or from the feet in the attempts to make cultures?

DR. RAPP. Both.

DR. WEIDMAN: We have commonly experienced difficulty in getting fungus from the hands. It is always necessary to make a number of attempts. I agree with Dr. Wright that this may be one of those "staphylococcic" cases. Other organisms besides fungi can produce eczematoid eruptions on the feet, and I do not think we ought to disregard that fact.

DR. CHAMBERS: I would like to suggest the opening of these vesicles and pustules surgically and, after evacuation of the pus, the use of 1:4,000 potas-

sium permanganate fomentations in conjunction with the routine treatment for fungus. I cannot help feeling that fungus may be present even though the culture is negative.

A Case for Diagnosis. Presented by Dr. Cross for Dr. Schamberg.

This young man has a circular, well defined, linear, papular lesion on the penis, which began about six months prior to presentation. Pruritus with some inflammation about the anus began about the same time. His Wassermann test is negative. On the glans, there are several papular lesions varying in size from that of a pinhead to that of a large pea. These are slightly firm on palpation and dull red.

DISCUSSION

Dr. Schildkraut: I venture the diagnosis of psoriasis of the penis.

Dr. Strauss: I suggest seborrheic dermatitis.

Dr. Weidman: I believe the condition is psoriasis, far-fetched as this diagnosis may seem. I was trying first to diagnose lupus erythematosus, but after seeing the lesion on the shin, I feel convinced that it is psoriasis. I think the infiltration is rather too deep and too edematous to be a seborrheic dermatitis; it is not superficial enough for that. As it is rolled between the finger and thumb, a dense stratum of infiltration which is close to the surface can be felt. I would like to have this put on the list of follow-up cases to be reported later.

Dr. Wright: It seems to me this case requires careful analysis before one can come to a conclusion. If this is a seborrheic dermatitis, it would certainly be most unusual for it to begin on the penis without any being present on the scalp or chest or the usual locations. As to the diagnosis of lupus erythematosus, there is a superficial resemblance, but there is no tendency to atrophy and no adherent scale; of course, the warmth of the place might account for that, but I would be inclined to agree with the diagnosis of psoriasis. There can be isolated spots of psoriasis any place, and the lesions have the clinical appearance of that condition. Furthermore, the pea-sized lesion on the lower leg is typically psoriatic.

Dr. Brown: By way of variation, I think lichen planus should be considered here. When seen under good light, one lesion particularly presented quite a flat top, and lichen planus on the penis is not unusual; that diagnosis should be kept in mind.

Dr. Chambers: I would like to agree with the suggestion that has been made of the possibility of the condition being lichen planus. I did not find any lichen planus lesions elsewhere, but the lesions on the penis could be papules of lichen planus.

Dr. Greenbaum: I saw this patient several days ago, and the question of psoriasis, seborrheic dermatitis, lichen planus, etc., came up. I think the man has psoriasis, but he likewise has an anal pruritis. Microscopic studies have not been made. He has one lesion on the left leg that is more or less typical of a psoriatic lesion.

Erythema Induratum. Presented by Dr. Schildkraut.

A woman, aged 24, presented a symmetrical eruption on her legs of six years' duration, consisting of nummular, bluish-red, symmetrical patches, some of which were infiltrated. Six years ago, she was in a poor physical condition, and at that time she was thought to have tuberculosis. Some of these lesions appeared at that time, and she has never been entirely free from them since, new crops appearing at intervals.

DISCUSSION

Dr. Weidman: This seems to be one of these intermediate cases between erythema induratum and erythema nodosum—that group which is included in one classification of sarcoid. I say intermediate case because the lesions have never

ulcerated, and the patient complains of tenderness, which is suggestive of erythema nodosum. I do not think that one should always expect every sign and symptom of a clinical complex to be present in every case, and that one should look for intermediate forms once in a while. I would suggest that this is a case, probably tuberculous at the basis, that lacks the typical appearance of erythema induratum.

DR. SCHAMBERG: I did not have the opportunity of hearing the history in this case, but I had a glimpse of the patient. I appreciate what Dr. Weidman has said, that there are certain features of the case suggestive of an atypical erythema induratum, but I have seen cases of erythema induratum in which the lesions were exquisitely painful, and in which the slightest touch caused evidences of distress; some cases are associated with a great degree of inflammatory reaction, as in this case. I do not think it is essential that the lesions should undergo ulceration; some cases run an indolent course, and the lesions disappear by resorption. I am rather inclined to believe that the condition in this case should be diagnosed as erythema induratum, despite the features referred to by Dr. Weidman.

DR. HIRSHLER: The extraordinary number of lesions appealed to me. Another interesting point in the diagnosis is that there are more lesions on the lower part of the extremities. In erythema nodosum, one is more apt to see the lesions, when they are so numerous, further up the leg or on some other part of the body. This bluish color that seems to be persistent is more significant of erythema induratum than of erythema nodosum.

DR. GREENBAUM: Despite the excellent results obtained with gold compounds in lupus erythematosus, considerable evidence has been brought forth against its use in tuberculosis. I wish to report on a case of erythema induratum, however, that I showed here. The condition subsequently cleared up after the administration of gold compounds and sodium thiosulphate, and did not recur, although it had done so after the administration of small doses of neoarsphenamine.

THE NEW YORK DERMATOLOGICAL SOCIETY

Regular Meeting, May 15, 1928

JOHN E. LANE, M.D., *President*

PAUL E. BECHET, M.D., *Secretary*

MYCOSIS FUNGOIDES. Presented by DR. WISE.

L. S., a single woman, aged 44, a clerk, presented an eruption which had begun as an erythematous pruritic plaque on the lower part of the back two years before presentation. Shortly after, similar red and violaceous, somewhat elevated patches appeared on both thighs from the groins to the knees. More recently, a group of irregular, somewhat firm, flat, discoid lesions developed on the inner aspect of the left upper arm.

The eruption consisted of numerous erythematous plaques of irregular outline from 1 to 8 inches (2.5 to 20.32 cm.) in diameter. They were located chiefly on the anterior, outer and inner aspects of the thighs, with scattered lesions on the groins and upper arms, and on both hips. The lesions were elevated, sharply defined and slightly scaly; the color varied from pink to violaceous. In some of the lesions on the thighs, infiltration and edema were well developed. Areas of unaffected skin, within some of the larger plaques, occurred mainly on the inner and upper aspect of the thighs. Itching had been severe, but had abated considerably under roentgen-ray treatment and injections of sodium arsenate, 2 per cent solution.

A section from one of the lesions on the thighs revealed the characteristic polymorphous infiltration in the corium, the lower border of the infiltration being sharply defined as an almost straight line. A large proportion of the infiltrating cells consisted of fibroblasts and large collections of well-staining mast cells.

A section of the tissue was presented with the patient. There was no adenopathy. The blood count and hemoglobin index were within normal limits.

DISCUSSION

DR. HIGHMAN: Clinically, the patient has mycosis fungoides. The nature of mycosis fungoides is not known, whether purely neoplastic or infectious, or something not yet identified. One characteristic of mycosis fungoides is the polymorphic infiltration, which the slide in this case presents. On the whole, I should be the more inclined to consider it mycosis fungoides because of the great variety of cells found in the infiltration.

DR. FOX: Clinically, I think that the case is unquestionably mycosis fungoides. The plaques show great variation in the amount of infiltration, there is a suggestion of circination, the patient complains of intense itching, and there has been improvement under roentgen-ray treatment. I am struck by the great number of cases of apparent mycosis fungoides of the early stages, compared with the few in the terminal or tumor stage. That some of the early eruptions are mistakes in diagnosis seems possible. Many of us have hospital connections which give us opportunities to see the terminal stages of this disease, but in my experience this is not at all common.

DR. WILLIAMS: Dr. Fox's remark reminds me of the old story that mules never die, for we never see a dead mule.

DR. TRAUB: I agree with the diagnosis. Another point in its favor is the fact that the skin between the lesions is apparently normal.

DR. WISE: I think Dr. Fox's remarks worthy of consideration, and there is no reason why we should not conceive of mycosis fungoides as occurring in relatively benign and in malignant forms.

DR. MACKEE: It has been my unfortunate experience to see more patients in the fungoid than in the prefungoid stage, and most of them have died in less than five years, although a few have lived for many years. While Dr. Fox's suggestion should be borne in mind, I am inclined to think that patients in the early stages go from one dermatologist to another and eventually consult some one when the lesion has become malignant.

TERTIARY SYPHILIS. Presented by DR. ELLER.

A. B., a housewife, aged 33, from the New York Post-Graduate Hospital, presented a lesion on the middle of the left side of the back. The patch was serpiginous, 6 inches (15.24 cm.) in diameter, slightly indurated and contained many red, ulcerated nodules, punched-out ulcers and scar tissue. The microscopic report confirmed the diagnosis of tertiary syphilis.

A CASE FOR DIAGNOSIS: BULLOUS ERUPTION OF THE FOREARMS. Presented by DR. FOX.

R. T., a woman, aged 64, born in Italy, had suffered from the eruption for three weeks. It was confined chiefly to the forearms, especially to the flexor surfaces. It consisted of various sized vesicles and bullae, some tense, others flaccid, the majority filled with clear serum, while a few were hemorrhagic. Some of the lesions showed an erythematous halo; others arose from normal skin. There were also a few vesicles, the size of a pinhead, on the cutaneous surface of the lips. There was no evidence of scratching, and the patient said that there was no itching. There was no history of the ingestion of drugs or injections of vaccines and serums. She did not come in contact with plants or

chemical irritants, except soap and cleansing agents. The hands were not affected, and the mucous membranes of the mouth were normal. She had not lost weight, and appeared to be in good health.

DISCUSSION

DR. MALONEY: A week ago there was more erythema than at the present time, and I thought that it was a case of erythema multiforme bullosum. There were then, however, as there are today, many bullae arising from the normal skin suggesting a possible pemphigus. I still think that it is a case of erythema multiforme bullosum.

DR. MACKEE: I am unable to make a diagnosis. One must think, as Dr. Fox did, of several possibilities, such as an eruption produced by drugs, erythema multiforme, pemphigus and dermatitis venenata.

DR. BECHET: I agree with the remarks of Dr. MacKee.

NODULAR SYPHILIDE RESEMBLING ECTHYMA IN A CHILD. Presented by DR. FOX.

B. F., a girl, aged 9, had suffered from the eruption for the past year. She presented ten lesions situated asymmetrically on the trunk and extremities. They varied in size from that of a ten cent piece to that of a silver dollar. All were sharply bordered and did not show evidence of scratching. Some were crusted and suggested ecthyma or possibly an eruption produced by bromide. A few nodules and some scarring were present. The Wassermann reaction was strongly positive. There was not any history of acquired syphilis and there were no stigmas of congenital syphilis or other apparent abnormalities, with the exception of the eruption.

DISCUSSION

DR. WHITEHOUSE: In considering the lesions themselves, I would have said it was a syphilid, in a moderately late stage. It is too symmetrical to be an extremely late syphilid. I am inclined to think it is an acquired infection. I do not know that I have seen nodular lesions of this sort in a congenital syphilitic patient. It is probably acquired.

DR. HIGHMAN: I think that it is difficult to say whether such a case is congenital or acquired. I do not know how it can be done without penetrating study. If acquired, it would be from 3 to 8 or 9 years old, dating back to infancy. In connection with congenital syphilis, it would be interesting if some one would some time classify the number of cases of congenital syphilis without stigmas. We may be much misled in either direction by overemphasis of the stigmas of congenital syphilis.

DR. MACKEE: I agree with Dr. Highman that it is probably impossible to determine whether in this case we are dealing with acquired or congenital syphilis. Certainly lesions of rupial syphilis are more common in acquired than in congenital syphilis; but, also, lesions of this kind can occur in congenital syphilis, and have done so. More information is necessary before the question can be decided.

DR. FOX: In my opinion, this may be either acquired or congenital syphilis. In the so-called syphilis congenita tarda, it is possible to have lesions practically identical with those seen in the acquired type of the disease. We intend to have Wassermann tests performed on the patient's parents, brothers and sisters, if possible.

MULTIPLE BENIGN TUMOR-LIKE NEW GROWTHS OF THE SKIN (SCHWENINGER AND BUZZI). Presented by DR. CLARK.

R. W., a housewife, aged 49, was presented before the Dermatological Section, New York Academy of Medicine, on May 11, 1928.

DISCUSSION

DR. HIGHMAN: The first time I heard the name of this disease, I believe, was when Pusey reported a case at the American Dermatological Association in 1917, and when he presented photographs and photomicrographs it struck me that it was a macular atrophy. I was all the more convinced of this similarity in Dr. Clark's case. It has all the clinical characteristics—the hernia-like capsules, the violaceous border, and the histologic observations are those of macular atrophy, of which Schweninger and Buzzi's disease appears to be a variety.

DR. WISE: I am not acquainted with the histologic observations in the Schweninger and Buzzi disease, but would be inclined to regard this as a macular atrophy. I do not see any evidence of tumor formation, although it may have been at one time a tumor-like disease. At present it is an atrophy of the skin. I would call it disseminated macular atrophy.

DR. FOX: I agree with the opinion of Dr. Wise.

DR. WHITEHOUSE: I agree with Dr. Wise and Dr. Highman.

LUPUS TUMIDUS. Presented by DR. ELLER.

A. B., a girl, aged 10, a patient of Dr. Ochs from the Post-Graduate Clinic, born in Persia, presented a nasal condition of four months' duration. The entire end of the nose was greatly enlarged, bulbous and purplish brown. There were a few tiny nodules suggestive of the apple-jelly type. The nasal mucous membranes were uninvolved and subjective symptoms were lacking. The Wassermann reaction had not yet been reported. A roentgenogram of the chest was negative for tuberculosis.

DISCUSSION

DR. CLARK: With the diascope I saw a few cuplike depressions, such as are found in lupus vulgaris. I cannot make a differential diagnosis between lupus vulgaris and syphilis in this case. The lesions around the orifice of the nose suggest syphilis somewhat.

DR. HIGHMAN: I think that this lesion is a gumma. I do not see the outstanding characteristics of lupus tumidus. Lupus tumidus is a rare form of tuberculosis at best, and is usually on the lobes of the ears where the return circulation is obstructed. The nose is too conspicious and important an organ to waste time in deliberation over diagnosis, when whether it is syphilis or tuberculosis can be determined by therapy. It seems to me that the therapeutic diagnostic test should be performed promptly.

DR. MACKEE: The rapid evolution, the infiltration of the entire nose and the absence of lesions on the mucosa are in favor of gumma. The age of the patient, the color and the possible apple-jelly nodules are in favor of lupus. I cannot make a clinical differentiation. Therapeutic and laboratory tests must and will be made.

DR. WISE: I strongly favor the diagnosis of lupus tumidus on account of the color, the soft boggy feel, the absence of scaling and the fact that I discovered, on diascopic pressure, apple-jelly nodules within the diseased tissue.

DR. FOX: I did not look at the lesions with a diascope, but without this I would make a probable diagnosis of lupus vulgaris. The case goes to show that late syphilis and lupus are extremely hard to differentiate, when the members of a body like this take diametrically opposite points of view.

DR. WHITEHOUSE: I agree with the majority of the speakers as to the probability of the condition being lupus vulgaris. Of course, it is rather rapid—four months—but coming around the orifice of the nose, I feel with the other speakers that syphilis should be ruled out with a therapeutic test.

DR. BECHET: I believe the condition to be lupus tumidus, but Dr. Highman's suggestion should be acted on and a therapeutic test given. It does not, however,

fit my conception of lupus tumidus; while the lesion is raised, it lacks the hyperplasic pachyderma of typical lupus tumidus.

DR. HIGHMAN: One of the things that has puzzled me is the diagnostic value of the apple-jelly nodules. When they are cleancut, there is no doubt of their significance; but we see them in lupus erythematosus, in which they represent agglomerations of altered elastic tissue, and, irrespective of the nature of the lesions in any tensed swelling of the face, they may be seen when pressed on with a diascope, and may be only sebaceous glands. It is possible that in a girl approaching puberty this might be what was noted, the swelling being a gumma. However, I did not notice them in this girl. I would like to hear some remarks about a diagnostic sign on which we lay great stress, often, it seems to me, without reflection.

DR. LANE: My impression is that this is lupus. It seems to me that tumidus is the proper appellation. In the few cases of rapidly growing lupus tumidus that I have seen there have been few of the so-called apple-jelly nodules. I do not know whether that has anything to do with the rapid growth, but in other varieties they are more plentiful than in rapidly developing lupus tumidus.

TUBERCULOSIS CUTIS. Presented by DR. TRAUB.

B. S., a negro housewife, aged 36, a native of Virginia, appeared at the New York Skin and Cancer Hospital, service of Dr. Williams, complaining of a generalized eruption, present for the past seven years. The family history was negative. She had been married sixteen years to a presumably healthy husband, and had not been pregnant. She complained a great deal about "womb trouble," and had irregular menses. About seven years before presentation, the patient had noticed a swelling under the right arm. Within six months this had disappeared, and a scaly eruption had appeared on the hands, then on the face, slowly spreading to the elbows, knees, arms and legs. The disease had been progressive from the start, leaving scars, had not produced any symptoms, and had been resistant to any treatment. Four years prior to presentation, the second and third fingers of both hands became swollen and slightly painful, but the pain soon disappeared leaving the fingers in their present state.

On presentation, the patient showed areas of scaling in the scalp, painful when removed. On the cheeks there was a circinate, apparently progressive, scaly and papular eruption, which left punctate scars and pigment in its wake. There was a scaly, verrucous-like eruption on the tip of the nose, and a circinate papular eruption around the alae of the nose and the edges of the lips and eyelids. On the left buttock, the elbows and the knees, there were large hypertrophic areas of eruption having a scalloped border. There were smaller similar areas on the arms and legs. The second and third fingers had the appearance of a spindle, and the tips were hooked palmward. There were a few macular and scaly areas on the palms.

The examination of the hands did not show any evidence of lesions that suggested tuberculosis or syphilis. There were changes that suggested trophic lesions, there being absorption of the cartilage of the distal phalangeal joints with lessening of the width of the joint space. There was a small amount of absorption of the bone along the cortical borders of the shafts of the middle phalanges of the third, fourth and fifth fingers. In the chest there was a little thickening of the interlobar pleura between the upper and middle lobes of the right lung, but no conditions in the parenchyma that suggested tuberculosis.

DISCUSSION

DR. HIGHMAN: I have seen disseminated, late rupial syphiloderms that looked like tuberculosis, as syphilis indeed often does, in patients with a negative Wassermann reaction, and at the risk of growing monotonous I would suggest antisyphilitic treatment for diagnostic purposes.

DR. MACKEE: I think that it is disseminate lupus, but in a case of this kind we must exclude syphilis.

DR. WILLIAMS: When I first saw the case I thought it was syphilis. I always examine the patients without the history and get my first impression purely on the examination. The healing in the center, and the scarring impressed me as a rupial syphilid, but on going into the history, the long duration with absence of any great amount of destruction changed my mind, and I now believe that it is tuberculosis.

DR. FOX: I think that the condition is tuberculous, on objective grounds.

DR. WHITEHOUSE: I think that the roentgenogram confirms the diagnosis of tuberculosis—the essential absorption and the shortening of the digits is rather characteristic of tuberculosis as seen in cases of sclerodactalia.

DR. CLARK: I think that it is a case of syphilis. It is unusual to see such lesions of tuberculosis, as the lesions we see here around the orifice of the mouth and the alae. I should expect those lesions to clear up under antisyphilitic treatment despite the negative Wassermann reaction.

DR. MACKEE: It seems to me that the location and character of the nodules compel the diagnosis of tuberculosis—the grouped, small nodules around the alae and on the lips; they look like the lesions of so-called lupus miliaris, which occurs only in the colored race around the nose and mouth and on the forehead. I have never seen such a picture in syphilis.

DR. TRAUB: Dr. MacKee has just mentioned the important points that make the diagnosis of tuberculosis. This patient presents heaped up hypertrophic crusts, not the shell-like scaling of a rupial syphilid.

DR. FOX: It is possible for lupus to assume the hypertrophic nodular and serpiginous type closely simulating syphilis. I presented such a case before the Academy Section, in which all of those who took part in the discussion appeared certain that the disease was syphilis. The condition failed, however, to respond to intensive antisyphilitic treatment, and the diagnosis was eventually proved conclusively by animal inoculation.

DR. TRAUB: We have taken two sections and will report later on the histology.

NOTE.—The report later showed typical tuberculosis cutis.

PERIPHLEBITIS NODULARIS NECROTICANS. Presented by DR. ELLER.

C. G., a woman, born in Hungary, aged 24, a hemstitcher, came to the Post-Graduate Clinic on May 12, 1928, complaining of an eruption on the lower extremities of two years' duration.

Examination revealed many scattered, irregularly placed, reddish elevations, some showing a tendency to linear formation. Some were painful on pressure. They varied in size from that of a pea to that of large bean. The extremities were cold and bluish.

DISCUSSION

DR. MACKEE: The case is one of Bazin's disease, with a legend of periphlebitis nodularis necroticans, simply because Lewandowski reported cases of this kind in which the lesions were small, deep and were situated on all aspects of the legs. The pathologic condition is perhaps a little less tuberculous and the infiltrations confined more to the deep vessels than in Bazin's disease, if that is possible. In Germany, I believe that periphlebitis nodularis necroticans is considered an entity, while in this country, where we are less inclined to be particular about relatively unimportant facts, the disease is known as Bazin's disease or an aberrant type of Bazin's disease.

DR. WHITEHOUSE: I agree that Bazin's disease is the type of eruption this patient exhibits.

DR. HIGHMAN: Why call it periphlebitis nodularis necroticans? Bazin's disease is a perivascular infiltration, and for a good reason. The infiltration cannot escape blood vessels. In fact, a characteristic feature of Bazin's disease is the relation of the infiltration to blood vessels. A name like this is another example of complicating dermatology in the most fatuous manner possible. It is unjustifiable by fact or necessity.

DR. BECHET: I agree with Dr. Highman that it is an aberrant type of Bazin's disease. I think that the name of Bazin's disease is better than the one presented. Dermatologic nomenclature is sufficiently complicated as it is, without needlessly adding such a long name in describing an aberrant type of a well known entity in dermatology.

LINEAE ALBICANTES. Presented by DR. TRAUB.

G. R., a stenographer, aged 18, American, appeared at the clinic of the New York Skin and Cancer Hospital, service of Dr. Williams, complaining of an eruption on the inner sides of the legs. Within the last few few months there had been a sudden gain in weight. Two months prior to presentation the patient had noted a few rounded, reddish areas on the inner side of the knees, and a few weeks later similar areas had developed on the upper leg. These had persisted, but had not produced any subjective symptoms.

On presentation, there were linear, somewhat tortuous, slightly hypertrophic areas on the inner sides of the upper legs. The skin in these areas was smooth and glistening. There seemed to be a slight excess in subcutaneous fat. A biopsy had been taken but not yet reported.

GRAY RUGAE OF THE HARD PALATE. Presented by DR. FOX.

J. K., a waiter, aged 33, born in Greece, had first noticed an abnormality of the hard palate three years before presentation. He was referred from the Manhattan Eye, Ear and Throat Hospital for an opinion on this condition. It consisted of several rows of narrow ridges, varying from ⅛ to ½ inch (0.3 to 1.27 cm.) in length. These ridges, or rugae, were firm and whitish, and were situated in the anterior third of the hard palate. There was a whitish hue to the entire hard palate, the soft palate appearing normally red. There was neither tenderness, nor subjective symptoms. There was no history of syphilis, and nothing to suggest ordinary leukoplakia. The patient had always been in good health and was a constant cigaret smoker.

DISCUSSION

DR. FOX: I am glad to learn that several of the members have observed this condition to which my attention had not been previously drawn. A brief search of dermatological textbooks and three books on diseases of the mouth did not disclose reference to it. The condition in this patient was accidentally noted three years ago. Whether it had been present from birth, I do not know.

DR. LANE: I have seen half a dozen of these anomalies of the mouth. They appear to be either congenital or rugae exaggerated by inflammation, frequently in smokers.

DR. WHITEHOUSE: I have seen such rugae from excessive smoking, and this man is a smoker. There are some rugae there normally, but they are often exaggerated by the heat of smoking.

RADIODERMATITIS IN A MAN AFTER ROENTGEN-RAY EPILATION OF THE BEARD FOR COSMETIC PURPOSES. Presented by DR. BECHET.

I. S., a man, aged 26, stated that he had wished to have removed a rather heavy beard, thereby relieving himself of the trouble of shaving. He had

received, according to his statements, forty treatments at one of the branches of an institute devoted to the epilation of hair by means of the roentgen ray. His chin and neck were a mass of telangiectasia and atrophy, thereby causing a formidable deformity; and strange as it may seem, he had lost only a moderate proportion of his beard.

DISCUSSION

DR. FOX: The question of preventing these "Tricho" or other advertising institutions from using the roentgen ray for treating hypetrichosis cannot be settled unless reports on bad results, which we are seeing in increasing numbers, are sent to Dr. Cramp of the Bureau of Investigation of the American Medical Association. Last week, while in Syracuse, I heard of four bad results from this method of treatment.

DR. CLARK: This is the third case I have seen that has been treated in this Institute in New York with this end-result. It is astonishing to me that men should seek this treatment.

A CASE FOR DIAGNOSIS. DERMATITIS VEGETANS? Presented by DR. TRAUB.

W. A., a man, aged 58, born in the United States, was first seen on April 27, 1928. His past history was negative, except that fourteen years before presentation he had had a condition of the skin diagnosed as eczema, which lasted about six months and had not recurred until about June, 1926. When presented, he had a general erythroderma and exfoliation, with marked thickening and exudation on the arms, legs and over the sacral region. The Wassermann reaction was negative. The blood count showed: 4,200,000 red blood cells; 14,000 white blood cells; hemoglobin, 78 per cent, and a color index of 0.92. The differential count was as follows: polymorphonuclear neutrophils, 71 per cent; small lymphocytes, 21 per cent; large mononuclear leukocytes, 4 per cent; eosinophils, 3 per cent, and basophils, 1 per cent. The biopsy report was as follows: Section showed epidermis with a marked acanthosis and cellular infiltration that extended throughout the corium and into the base of the follicles of the hair. There were numerous dilated blood vessels. The appearance in the upper third of the corium was almost that of granulation tissue. Some of the cells contained almost black pigment granules. On the surface, there were two vesicles filled with serum and white blood cells. The infiltration was composed of plasma cells.

The patient had improved materially on the administration of alkaline baths and fractional roentgen-ray treatments. He had received four injections of sodium thiosulphate, but refused to continue the treatment.

DISCUSSION

DR. WISE: From the appearance of the patient's skin at present, I would make a diagnosis of universal erythroderma and secondary lichenification.

DR. TRAUB: I agree with Dr. Wise that you can name this condition, but that does not mean anything.

DR. CLARK: I would like to find out more about it. The general picture is like a great many of those chronic arsenical cases that Dr. Throne and Dr. Myers have had in our clinic at the Skin and Cancer Hospital, with considerable thickening and lichenification. The fact that the man had four injections of sodium thiosulphate and then had the same in pill form means nothing. It would probably require injections of sodium thiosulphate for two or three months before he would get any real therapeutic effect. I do not think that they have exhausted arsenical treatment in this case. I should like to see the man given that treatment—I have seen so many cases in which the condition has entirely cleared up. Recently, I treated a man with an eruption just like this. I have been working on him for three months and for a long time he did not

make any improvement, but constantly showed arsenic in the urine. Now he is improving; the skin is better, less thickened and the itching is greatly lessened.

DR. HIGHMAN: Clinically and histologically, the observations substantiate Dr. Wise's diagnosis. Clinically and histologically, there is not any resemblance to dermatitis vegetans, which resembles pemphigus vegetans, as the lesions in this case do not. In other words, the picture of dermatitis vegetans is vegetating granulation tissue. There is no such thing here. I think it is lichenification tending to be verrucous. Whether it is primarily erythroderma or symptomatic, as of leukemia or a kindred thing, cannot be determined without further study.

DR. MACKEE: I agree with Dr. Highman. These cases are not uncommon and they sometimes end in the leukemic group. Many of them are secondary to some previous disorder, such as dermatophytosis or dermatitis venenata, or even psoriasis. Some of them seem to be toxic and allergic. Occasionally one is due to arsenic. It is absolutely necessary to keep these patients from rubbing and scratching. There is nothing specific to do as a rule. Such patients require great therapeutic skill. As a rule, the prognosis is favorable but it must be guarded.

DR. TRAUB: I apologized when I presented the case, for the appearance today is different from when I first saw the patient. The lesions then present have greatly improved, and do not so strongly suggest the diagnosis of leukemia, which first occurred to me. The man objected to treatment with thiosulphate, as he did not like the experience he had had with it.

LUPUS ERYTHEMATOUS LIMITED TO THE LOWER LIP. Presented by DR. BECHET.

B. M., a woman, aged 51, presented a sharply outlined, scaly lesion on the lower lip, which involved most of it, with somewhat atrophic areas in its center. The plaque was of a violaceous color. No other lesions, either on the face, ears or scalp, were discernible. The lesion had been present for five years.

DISCUSSION

DR. WILLIAMS: The condition may be lupus erythematosus, but I do not believe it possible for any one to make a positive diagnosis of lupus erythematosus when the only lesions are on the vermilion border of the lip.

DR. FOX: In my opinion, a positive diagnosis of lupus erythematosus could not be made from lesions limited to the vermilion border of the lip. I think, however, that this diagnosis is probably correct.

DR. HIGHMAN: I think that the condition is lupus erythematosus.

DR. WISE: I think that the condition is lupus erythematosus, on clinical grounds alone.

DR. BECHET: Dr. Wise's remark makes me happy, for while I realize the difficulty of making such a diagnosis when the lips alone are involved, nevertheless, I felt certain of it; lesions with scaling, sharply outlined margins, and somewhat atrophic center, were suggestive of no other condition. I will grant that it is unusual for lupus erythematosus to exist for five years on the lower lip alone, but the latter fact is not of sufficient importance to make negative the diagnosis.

TUBERCULOSIS CUTIS. Presented by DR. BECHET.

C. S., aged 56, had been presented before the Section on Dermatology and Syphilis, of the New York Academy of Medicine at its May, 1928, meeting, with the same diagnosis. At that time the diagnosis of Paget's disease was made by Professor Bloch of Zurich and by Dr. Pollitzer. Since then biopsy confirmed the diagnosis of tuberculosis cutis.

CHICAGO DERMATOLOGICAL SOCIETY

Regular Meeting, May 16, 1928

F. E. SENEAR, M.D., *President, Presiding*

URTICARIA PIGMENTOSA. Presented by DR. FINNERUD.

A girl, aged 6 months, had seventeen brown spots on the trunk and extremities which began to appear about three months before presentation. Apparent subjective symptoms were not present. Examination showed light brown lesions, some elevated and some flush with the surrounding normal skin, averaging about 1 cm. in diameter. The lesions urticated when they were rubbed.

DISCUSSION

DR. FINNERUD: I was glad to have the opportunity of presenting this patient with classic urticaria pigmentosa, because so many unusual pigmentary cases have been shown of late in which that diagnosis was considered.

A CASE FOR DIAGNOSIS. Presented by DR. SENEAR and DR. CORNBLEET.

C. A., a negro boy, aged 9, had an eruption which began behind the ears when he was 6 months of age. The condition had spread to the head, the face and thence down the trunk and extremities. At the time of presentation the eruption consisted of scaly, crusted, lichenified and verrucous patches, varying in size from that of a coin to that of a palm; there were also plaques on the extensor surfaces of the upper extremities, buttocks and on both the extensor and flexor surfaces of the lower extremities. Follicular keratoses were noted in the extensor surfaces in which the eruption had not occurred, and the skin over all areas was dry and harsh. On the right side of the chest and scattered among the other lesions were small grouped lichenoid lesions with hyperpigmented borders. Neither scars nor depigmented areas were noted. Itching was moderate, but was greater during the summer. The lymph glands of accessible chains were palpable and movable, discrete and of moderate size. Over each inguinal region was a tumor the size of a hen's egg, which was smooth, movable, resilient, neither painful nor tender and subcutaneous. The testicles were undescended. The left shoulder was higher than the right and was held tensely; there was a small lordosis and a greater left scoliosis. Objects were picked up from the floor with the trunk unflexed and the left shoulder thrown back. The child coughed at night, at times coughing up blood; he had frequent colds, tired easily and shrunk from playing with other children. A roentgenogram of the chest showed evidences of old tuberculosis of the hilum with some parenchymal involvement of the upper lobes of the lungs.

DISCUSSION

DR. H. R. FOERSTER: In spite of the extent of the eruption and its symmetry I feel that verrucous tuberculosis should be considered.

DR. ORMSBY: I have seen rather widespread verrucous lesions of tuberculosis, following a shower of nodules, form patches like these. This case can well be an example of verrucous tuberculosis.

DR. O. H. FOERSTER: I should like to ask about the experience of the members of the society with the incidence of glandular tuberculosis in this particular type of eruption as compared, for example, with pulmonary or osseous tuberculosis. It seems to me that the widespread types are more often seen in connection with glandular tuberculosis.

DR. STILLIANS: I think that these lesions are seldom seen in connection with pulmonary tuberculosis.

DR. WILE: In two cases of obscure tuberculosis in which we were entirely unable to find any focus of infection for a long time a roentgenogram, which was taken too high for the chest, revealed a calcified tubercular gland in the neck. I am convinced that in many of these cases the condition is due to old calcified glands, which show readily in the roentgenogram if the glands of the neck are photographed.

LUPUS PERNIO. Presented by DR. EBERT and DR. OMENS.

A Jewess, aged 42, had lesions which had appeared gradually during the past two years before examination. They did not cause any sensation except that the hands felt heavy at times. The color was more marked in winter. The family and personal histories were insignificant. Irregularly oval patches, the size of half a palm, were noted over each elbow; they were livid, bluish, a little raised and appeared somewhat puffy, shading off gradually into the surrounding skin. Definite nodules were palpable at the margins. On glass pressure, light yellow macules, the size of a pinhead, were visible. Somewhat smaller and less marked patches were present over the knees and the knuckles of both hands. The fingers were bluish red and somewhat puffy. There was a diffuse bluish infiltrate of the lower half of each leg, and a patch, the size of the thumbnail, over each buttock.

DISCUSSION

DR. O. H. FOERSTER: I think this case would go into the group of lupus pernios. The inflammatory features are marked. There seems to be a little atrophy, and there are some sharply bordered infiltrates. The whole process appears to be superficial.

DR. FINNERUD: I think that before ruling out acrodermatitis chronica atrophicans a biopsy should be performed, although the condition is probably some unusual tuberculous manifestation.

DR. EBERT: This is a private patient of Dr. Omens'. She is nervous and worried about her condition, and a complete examination has been impossible. We had a roentgenographic examination of the bones of the forearms and hands, thinking there might be changes in the bone such as are described in the literature, but none were found. We presented her with a tentative diagnosis of lupus pernio, and believe the picture corresponds fairly closely with the cases that have been described as that disorder, particularly in the German literature.

LICHEN PLANUS. Presented by DR. SENEAR.

A man, aged 41, reported that about six months before presentation he developed an eruption which began on the face and gradually spread over the trunk and extremities. The lesions were always of a brownish tint, and itching had been moderately severe. He was seen by a physician who thought his condition was due to syphilis, and he received twelve injections of neoarsphenamine. Examination revealed a profuse eruption of brownish macules, varying in size from that of a pinhead to that of a dime, on the scalp and face, those in the latter location involving principally the forehead, nose and preauricular region. The neck, trunk and upper extremities also showed numerous lesions of similar type. The eruption was not profuse on the forearms, but the lesions present involved particularly the flexor surfaces of the wrists. In places the lesions had a definite linear arrangement, and many of them showed an annular configuration. While most of the lesions seemed to be purely pigmentary, a few of them were a dusky red. On the flexor surface of the left forearm was a single, burnished papule, the size of a pinhead, typical of lichen planus. There was a definite atrophy in

some of the lesions on the face, forearms and trunk. The buccal mucosa and dorsum of the tongue showed a few, typical, whitish patches of lichen planus, some of them having annular configuration.

DISCUSSION

DR. ORMSBY: I think that it is unusual to have pigmentation of the scalp in lichen planus, although I have seen it on the forehead. It may be that the pigmentation was increased by the therapy. Sometimes when arsenic is given orally or by injection extensive hyperpigmentation results, and this may have been a factor in this case.

DR. ZEISLER: The French, particularly, seem to be enthusiastic about the use of neoarsphenamine in treatment of patients with lichen planus, and I think the pigmentation is much more likely to remain after such therapy.

DR. H. R. FOERSTER: I would like to know whether Dr. Lieberthal thought this patient also had syphilis.

DR. SENEAR: Dr. Oliver and I examined this patient together, and felt that the whole picture was that of lichen planus. In some areas the man has eight or ten of the small lesions together; my feeling is that the entire picture is due to lichen planus, and that the arsenic probably had something to do with the formation of the pigmentation.

A CASE FOR DIAGNOSIS. Presented by DR. EBERT.

A negress, aged 32, presented two distinct disorders of the skin: Numerous, flat, papular lesions on the legs, and a few scattered over other areas, had been present as long as she could recall and had not caused any discomfort. Her father, a brother, aged 25, and a sister, aged 36, had had similar lesions since infancy, which had not changed in character. In December, 1927, reddish lumps appeared on the shins which later discharged pus, and then disappeared leaving the pigmented relics now evident. A few of these lesions were still active. This eruption was associated with frontal headaches and general malaise. About this time the nailplate became separated distally from the nailbed on the first three fingers of the right hand and on the first and third on the left hand. She said that the nails appeared purple, as though bruised, in the area involved.

She was married six years before presentation and had never been pregnant. She was operated on for pus tubes eight years prior to presentation. She complained of leukorrhea and dysmenorrhea. The Wassermann reaction of the blood was positive. She had received two injections of neoarsphenamine during the past ten days, without any effect on the eruption. On both shins there were numerous closely set, flat-topped papules, varying in size from that of the head of a match to that of a coffee bean, which were slightly raised and polygonal in outline. When palpated they had a more parchment-like texture than the normal skin. They were less pigmented than the surrounding skin and appeared slightly waxy. On the calves and lower part of the legs the lesions were smaller, more closely set and round or oval. A few of these lesions were grouped over the sacrum and on each side of a midabdominal operative scar; a few were scattered over the trunk, arms and back of the fingers. In addition, there were one or two subcutaneous nodules, the size of a bean, on each calf. The skin over these areas was reddened. There were several pigmented relics, especially on the shins. There was a group of small crusted papules, the size of a half dollar, on the dorsum of the left foot arranged in a semicircle. The diseased nails were separated for the distal one-third, and there was a space of 2 mm. between the plate and the nailbed, which was keratotic and thickened. The nailplate itself was thinned. The nail on both large toes was dystrophic.

A biopsy was taken from a flat papule on the leg. In a section stained with hematoxylin and eosin the following histologic changes were noted: In the

involved area the epidermis was thickened, and the papillae were completely flattened out. The upper half of the corium was made up of fibers which were unusually fine and stained lightly with eosin. Hairs or sweat glands were not present. The connective tissue nuclei seemed larger and paler than normal. On the lower half of the corium the sweat glands appeared normal. Sections were stained with Weigert's elastic tissue stain. There was a complete lack of elastic tissue in the involved upper half of the corium, while in the rest of the section it stained normally.

DISCUSSION

DR. WILE: I have never seen anything like the condition in this case. Some of the lesions on the leg which at first glance were suggestive of lichen planus on further observation did not fit in with that disease. There was not any evidence of pruritus.

DR. ZEISLER: I suggest the diagnosis of Unna's cardlike scleroderma.

DR. H. R. FOERSTER: I wish to suggest for consideration a form of colloid degeneration of the skin. The section showed densely packed collagen much of which took the basic stain, and I think it may be an early stage of colloid degeneration.

DR. ORMSBY: We considered some type of degeneration in this case. Dr. Zeisler's suggestion of localized scleroderma is corroborated by the histologic examination.

DR. EBERT: My discussion must be speculative, and I can say only that further work will be done to determine whether or not a degenerative process is present.

DR. WILE: I think that there is a great deal of evidence against this being a degenerative process. In the first place, there is a regularity of distribution which one does not usually associate with degenerative processes. Second, the lesions were raised and papular. Most of the cases of colloid degeneration, except one or two that are unique, have been associated with atrophy so that the skin has been wrinkled, particularly in the keloid degeneration of the forehead and that seen occasionally in the groin and around the breasts. If this were a degenerative process, simple colloid degeneration, the only way one could account for the papular nature of the process would be to assume that it exists because of hypertrophy of the colloid tissue, and ordinarily degenerating tissue does not react in that way.

LICHEN PLANUS ANNULARIS. Presented by DR. ORMSBY.

A man, aged 37, had a disorder of nine weeks' duration consisting of seven lesions, three on the right leg, one on the chest and three on the back, which varied in size from that of a split pea to that of a dime. These lesions were well defined, circular or oval, and each presented a threadlike, elevated margin. The center was smooth and slightly translucent and presented an occasional dilated blood vessel. Lesions did not appear elsewhere on the body and subjective symptoms were not demonstrated.

DISCUSSION

DR. STILLIANS: I think that it is a simple epithelioma.

DR. FINNERUD: I think that the case clinically is much like one I showed in a Japanese two or three years ago. Lichen planus was discussed in that case, although porokeratosis was considered. I sent sections to Dr. Engman, and he said he could not be sure about the diagnosis of lichen planus from the slides. There was a fine threadlike depression of the surface of some of the marginate lesions.

DR. MITCHELL: I was immediately struck by the resemblance of this case to the one shown by Dr. Finnerud several years ago. At that time I was inclined to doubt the diagnosis of porokeratosis, and I feel the same about this case. The fine line suggests an epithelioma, and I think the question must be decided on the histologic examination.

DR. ORMSBY: I think it is either an unusual annular lichen planus or an epithelioma, and agree that the diagnosis must be decided by the histology.

NOTE.—The histologic examination made subsequently revealed the typical picture of lichen planus.

KERION WITH LICHENOID TRICHOPHYTID. Presented by DR. OLIVER and DR. FINNERUD.

A negro boy, aged 3, entered the Cook County Hospital because of an eruption of the scalp of ten days' duration and a similar eruption of the body of four or five days' duration. Since the eruption had appeared on the body, the patient had not been sleeping well, and had no appetite, due to fever, the mother said. Examination showed a half dozen crusted, well elevated, boggy nodules of the occipital and parietal regions, varying in size from that of a split pea to that of a dollar, and numerous discrete and grouped minute follicular papules, pustules and vesicopapules of the face, trunk and upper extremities, most marked on the sides of the trunk. There was general adenopathy of the superficial lymph glands, most marked in the cervical region. Examination of the hair stumps of the scalp nodules in potassium hydroxide preparations showed the fungus.

DISCUSSION

DR. MITCHELL: I accept the diagnosis in this interesting case. I took out some hairs and will try to get a culture and determine what the organism is.

DR. FINNERUD: The eruption on the body in this patient is interesting. Some of the lesions are small papules, some are papulovesicles and some are papulopustules. When first seen, a few days ago, the eruption was much more extensive. The mother said that the lesions in the scalp had been present for only about ten days and that the eruption on the body has been present for about seven days. She did not mention the eruption on the body, but because the lesions on the scalp developed so rapidly we asked to have the boy undressed and found this trichophytid and a generalized lymphadenopathy.

TUBERCULOSIS (?). Presented by DR. SENEAR.

This patient was presented by Dr. Weber at the March meeting of this society, and the case is reported with the proceedings of that meeting in the ARCHIVES OF DERMATOLOGY AND SYPHILOLOGY.

DISCUSSION

DR. FINNERUD: From the microscopic sections I thought there was a greater likelihood of this being a syphilitic process than a tuberculous one. There was what resembled a miliary tubercle in two places in the section, and in one of them there were two giant cells, but because of the vascular involvement and what I definitely considered a hypertrophic change in the arterioles, I favor the diagnosis of syphilis rather than that of tuberculosis.

DR. WILE: Am I right in assuming that this patient had a high lymphocytic count? (Yes, 50 per cent). I would think this is not against a diagnosis of tuberculosis, and will point out that there are many cases on record of patients coming in with a picture of leukemia in the blood observations who at autopsy are found to have miliary tuberculosis. I think the differential diagnosis on the one section between tuberculosis and syphilis would be difficult, but in view of the high lymphocytic count and the chronicity of the process I would be in favor of systemic tuberculosis.

DR. O. H. FOERSTER: I think the history of alopecia with regrowth, and the entire clinical course so far would speak for syphilis rather than for any other process.

DR. SENEAR: I am much obliged for the suggestion made. Personally, I am inclined to agree with the point expressed by Dr. Foerster, particularly after the rapid response of the cutaneous lesions to the first injection of arsphenamine. I am inclined to think that the whole picture is syphilitic.

DR. WILE: It is fair to point out that this is not the type of alopecia one ordinarily finds in syphilis; also, that it has been present for several months. Has the patient any history of syphilis?

DR. SENEAR: No, there is no history of syphilis. We have had her examined by gynecologists, looking for cervical chancre, and while an erosion was found, they were not willing to commit themselves.

CASE FOR DIAGNOSIS. PIGMENTATION. Presented by DR. FINNERUD.

A Jewish boy, aged 13, reported at the Central Free Dispensary because of an eruption of the body of two and a half years' duration. Neither the patient nor his father knew anything about the onset of the eruption, both claiming that it was of its present appearance when first noticed. Besides measles at the age of 4 years, the patient had not had any skin disorders or serious illnesses. The discolored areas had never been red. The patient always took either milk of magnesia or "exlax" when troubled with constipation.

Examination showed numerous rather well defined round and oval bluish-brown macules of the trunk, arms and thighs, varying in size from that of a split-pea to that of a finger-nail. There was a livid reticular pattern of the forearms, hands, thighs, legs and feet, and the hands and feet were bluish red and colder than the skin elsewhere. The bluish-brown macules did not urticate when rubbed. Histologic sections from a macule of the trunk did not show any noteworthy change other than the presence of numerous chromatophores approximately at the junction of the papillary and reticular portions of the corium.

DISCUSSION

DR. ZEISLER: I think this is one of the cases in which a diagnosis can usually be made at a distance, and when we see the bluish spots we say "phenolphthalein."

DR. WILE: My impression was that these spots were due to body lice, which the patient probably had a couple of years ago, and that they are maculae cerulae. I used to see these cases frequently in New York, and it is proper to point out that these discolorations last for a tremendously long time after the parasite is no longer present. The fact that the patient has been taking exlax is suggestive evidence of eruption produced by phenolphthalein, but I would want to be sure that he did not have body lice when the condition started.

DR. FINNERUD: I am grateful for Dr. Wile's suggestion. I did not think it was an eruption caused by exlax, although all I have to go by is the history that the lesions are never red. I thought this case was similar in appearance to the one I showed a month ago, in which the pigmentation followed measles. We did not get a biopsy on that case but in this one we had a specimen, and the pigment granules were seen to be altogether within the corium, about at the junction of the papillary layer and the deeper part. I thought there was possibly some relation between these acquired cases of pigmentation of this character and the ordinary mongolian spots.

SECONDARY SARCOMA. Presented by DR. WEBER.

A man, aged 35, born in Germany, was shot in the left wrist in 1915. The wound healed readily. One year later the scar ulcerated and was curetted several

times, healed and remained well for five years, after which it again ulcerated. It again healed after another curettement, but remained well for only a few months. A section taken at that time indicated a malignant condition. Eighteen months before examination the man's arm had been amputated above the wrist.

About three months before presentation he developed a lesion on the upper lip, and at about the same time the left side of the upper jaw became sore. One tooth was extracted. Other nodules appeared one week after the first one. The lesions consisted of pearly nodules, smooth and glossy on the surface and peculiarly hard to the touch. The lesions were movable. Some of the nodules were situated in the corium and others below it. The cervical glands were enlarged.

DISCUSSION

DR. LIEBERTHAL: I examined the specimens and will accept the diagnosis without reserve. It is a spindle cell sarcoma.

DR. WEBER: The specimens were sent to Dr. McGlumphy and Dr. Zeit, and they agreed with the diagnosis of spindle cell sarcoma.

KAPOSI'S SARCOMA. Presented by DR. EBERT and DR. OMENS.

An Italian laborer, aged 42, four months before presentation noticed a small nodule over the inner condyle of the right ankle. This gradually increased in size, and similar nodules continued to appear. There had been no sensation, and none of the lesions had disappeared spontaneously. At present there were about two dozen nodules, varying in size from that of the head of a match to that of a small hazelnut, over the right inner condyle and on the median surface of the calf. These were bluish red, firm and hemispherical. There was a boardy edema of the ankles.

An histologic examination was made of one of the smaller nodules. The sections were stained with hematoxylin and eosin. The nodule was formed by a lens-shaped infiltrate in the upper half of the corium, which was fairly well demarcated from the surrounding corium and which was separated from the thinned, overlying epidermis by a thin layer of collagen. This infiltrate was made of strands, some of which were cut in long sections and some in cross-sections. Those cut longitudinally were rich in nuclei, which resembled rapidly growing connective tissue cells. The cytoplasm was scanty and indefinite. In cross-sections these nuclei were small, round and darkly stained. In the upper portion there were several large endothelial lined sinuses, while in other areas apparently newly formed, endothelial lined spaces of much smaller caliber, a little larger than capillaries, were noted. Hemorrhage was not seen.

DISCUSSION

DR. MITCHELL: I thought of a Kaposi and an ordinary sarcoma, but did not examine the lesions carefully enough to differentiate between the two.

DR. O. H. FOERSTER: I thought it was an early Kaposi's sarcoma on the legs and that the lesion on the back of the neck was an acne keloid.

DR. WILE: I agree with Dr. Foerster's diagnosis. The picture under the microscope was entirely consistent with the spindle cell sarcoma, which might be called an angiosarcoma.

DR. LIEBERTHAL: The lesions are minute, and I would suggest that some of them be removed and the change studied in the small capillaries. I am sure it will be found interesting.

DR. EBERT: The response to roentgenotherapy has been marked, and the picture is not so striking as when I first saw the patient a few weeks ago. We will attempt to follow Dr. Lieberthal's suggestion.

CLEVELAND DERMATOLOGICAL SOCIETY

H. J. PARKHURST, M.D., *Reporter*

Regular Meeting, May 24, 1928

CHARLES G. LAROCCO, M.D., *Presiding*

A CASE FOR DIAGNOSIS. Presented by DR. COLE and DR. DRIVER.

J. G., a man, aged 39, a laborer, had gone to the hospital three and one-half years before presentation for the treatment of a cough and "stomach trouble." While there, a polyneuritis had developed, which resulted in contractures of the extremities; although there had not been any history of arsenical medication, a generalized brownish pigmentation had appeared and persisted. As presented, the patient was markedly emaciated, with a generalized mottled pigmentation, especially on the trunk. There were a few small keratoses on the palms and soles. The mucous membranes were not involved. There was pronounced muscular atrophy of the extremities. The blood pressure was 84 systolic and 54 diastolic.

DISCUSSION

DR. MISKJIAN: The low blood pressure favors a diagnosis of Addison's disease, but the palmar keratoses seem to be of arsenical origin. Possibly this case represents a combination of the two conditions.

DR. CUMMER: Dr. Dexter, of this city, has studied groups of patients with Addison's disease, and has found the pigmentation especially in areas of skin bound tightly by the clothing. This case does not impress me as being one of Addison's disease.

DR. NETHERTON: The keratoses on the hands and feet are apparently arsenical in origin, and the pigmentation seems too dark for Addison's disease.

DR. RAUSCHKOLB: The mucous membranes in this case are not pigmented as they would be in Addison's disease.

DR. COLE: We know that arsenic can produce these cutaneous changes, but the low blood pressure still has to be explained.

PARESIS ASSOCIATED WITH CUTANEOUS AND OSSEOUS SYPHILIS. Presented by DR. COLE and DR. DRIVER.

A. R., aged 40, a steel worker, did not give a history of venereal diseases, and presented tertiary cutaneous lesions of eighteen months' duration. Roentgenologic studies of the hands showed periostitis with bone proliferation throughout; periostitis was also found in the ulnae, radii, tibiae and fibulae, but not in the skull. The Wassermann reaction of the blood and spinal fluid was strongly positive, and the spinal fluid cell count was 14; the globulin reaction was 2 plus, and the gum mastic curve was 4321000000.

MELANOCARCINOMA WITH GENERALIZED METASTASES. Presented by DR. COLE and DR. DRIVER.

F. U., a man, aged 51, a barber, had had a callus on the right great toe for many years; he had trimmed it away frequently. During the previous three or four years he had noticed a black spot in the callus, which had enlarged gradually. Thirteen months previously the toe had become quite painful and was apparently infected. It had failed to heal under topical applications, incision and drainage, and in October, 1927, the toe was amputated and right inguinal lymph nodes were removed. Two or three months later, many small red and black areas appeared along the course of the lymphatic vessels of the right leg and thigh. A swelling

appeared in the right groin and the stump of the toe broke down. Finally, attacks of jacksonian epilepsy appeared. The urine contained melanin. The patient's father had died at the age of 54 of a "fungating lesion of the chest."

VON RECKLINGHAUSEN'S DISEASE AND SARCOMA. Presented by DR. COLE and DR. DRIVER.

C. B., a man, aged 20, had had many small tumors in the skin since childhood. Ten years before presentation he had first noticed a soft tumor, about the size of an orange, under the skin of the right thigh. The patient was first seen in 1921. Since January, 1927, the tumor had enlarged rapidly, and in August, 1927, an attempt to remove it was unsuccessful. Its circumference was 44 inches (111.76 cm.).

DERMATITIS EXFOLIATIVA SECONDARY TO PSORIASIS. Presented by DR. COLE and DR. DRIVER.

C. F., a truck driver, aged 36, had first noticed a scaly lesion on the right shin thirteen years before presentation, and other similar lesions had appeared gradually over the entire body. The eruption had cleared up in several months, only to be followed by a fresh outbreak annually. A few lesions usually persisted throughout the year. One year before the time of presentation, an outbreak had appeared and had become generalized, an exfoliative dermatitis developing. The condition of the blood was nearly normal, except that there was an eosinophilia of 5 per cent.

DISCUSSION

DR. PARKHURST: The history and the punctate pitting of the nails point to a psoriatic origin.

DR. BARNEY: I agree that psoriasis was apparently the primary factor in this case. The case now presents the features of pityriasis rubra of Hebra, even including the adenopathy.

TUBERCULOSIS VERRUCOSA CUTIS ("DISSECTION TUBERCLE"). Presented by DR. COLE and DR. DRIVER.

S., a man, a pathologist, who did many autopsies, had injured his left forefinger slightly in August, 1927, after which a persistent verrucous lesion had developed.

DISCUSSION

DR. COLE: This is the first case in my experience that has not responded at once to roentgen irradiation.

TUBERCULOSIS CUTIS AND TUBERCULOUS DACTYLITIS. Presented by DR. COLE and DR. DRIVER.

M. K., a boy, aged 2 years and 6 months, had had lesions on the hands, legs and face for three months. Some had healed spontaneously. There had been little discomfort. Roentgenologic studies showed the presence of dactylitis in the proximal phalanx of the right middle finger, with periosteal proliferation. The tuberculin test was strongly positive (1 : 100,000).

DISCUSSION

DR. J. H. DAVIS: From the character of the tuberculin reaction and the fusiform swelling of the fingers, the condition may be diagnosed as tuberculous dactylitis with cutaneous tuberculosis.

DR. COLE: In this case the tuberculous infection seems to be blood borne. We have found that in children we must use small doses of tuberculin. As a

routine we start with 1:100,000. This child has developed a lichen scrofulosorum type of eruption, aggravated after tuberculin had been given.

SERPIGINOUS SYPHILID (?). Presented by DR. COLE and DR. DRIVER.

M. M., a white woman, aged 40, had noticed a small pink lesion on the right hand three and one-half years before presentation. The involvement had extended to the right forearm. One year previously, similar lesions had appeared on the left hand and on both thighs. Several times these had almost disappeared, only to recur more extensively. There had been occasional slight pruritus. A biopsy report had not yet been obtained. The Wassermann reaction was strongly positive.

LUPUS ERYTHEMATOSUS. Presented by DR. STEINBERG.

H., a woman, aged 24, born in Germany, had had a nasal operation a year before presentation, together with tonsillectomy. This had been followed by severe furunculosis, which had subsided. There were erythematosquamous patches on the face of six months' duration, and the mucous surfaces of the lips were involved. There were burning and itching sensations. There was not any personal or family history of tuberculosis, or any sign of the infection.

DISCUSSION

DR. FISHER: Exposure to the sunlight may have aggravated this case. I would suggest treatment with gold sodium thiosulphate.

A CASE FOR DIAGNOSIS: ERYTHEMA ELEVATUM DIUTINUM (?). Presented by DR. BARNEY.

K., a woman, aged 28, presented an eruption of ten days' duration, with pruritus, on the dorsa of the hands. On the right hand were six pea-sized to half palm-sized reddish brown plaques. Each lesion had a definite elevated round border, redder than the slightly depressed brownish center. There was not any scaling. There was slight palpable induration, especially of the borders. At the base of the left index finger on its extensor aspect was a pea-sized involuting lesion in the form of a brownish discoloration. On the radial surface of the left wrist was a similar involuting lesion.

DISCUSSION

DR. FISHER: She has taken phenolphthalein and olive tablets. I believe this causes the eruption.

DR. PARKHURST: The eruption seems to be too fleeting for erythema elevatum diutinum or granuloma annulare, which are probably synonymous. A phenolphthalein eruption is suggested, but the borders seem too elevated. Since the eruption followed a "cold," I would suggest a diagnosis of erythema multiforme, but it would seem advisable to administer a test dose of phenolphthalein later.

PEMPHIGUS VULGARIS. Presented by DR. STEINBERG.

H., a man, aged 55, born in the United States, had been a butcher for many years. Blisters had appeared in the mouth, and he had had all of his teeth extracted, but the lesions had continued to appear and had resisted various local applications. The umbilicus was involved, with crusting.

PITYRIASIS ROSEA WITH HERALD PATCH ON FOREHEAD. Presented by DR. FISHER.

A. J., a man, aged 30, presented an extensive brownish macular and scaling eruption on the face, neck and trunk, which had begun with an oval lesion on the forehead five days before presentation. There were other patches on the face that had developed subsequently.

A CASE FOR DIAGNOSIS: SOLID-EDEMA OF THE EYELIDS. Presented by DR. RAUSCHKOLB.

B. H., a negress, aged 38, had had a persistent swelling of the eyelids for two years, with recurrent attacks extending back for five years. Each outbreak had been preceded by a "cold," or some trouble with the ears or nose. Ethmoidal sinusitis had been found. Both eyelids, especially the lower, were considerably swollen, and pitted on pressure. Other physical observations were negative.

DISCUSSION

DR. PARKHURST: The areas seem erythematous. The condition accompanies "head colds," and suggests lymphatic infection as seen on the upper lip in some cases.

CUBA DERMATOLOGICAL ASSOCIATION

J. J. MESTRE, M.D., *Secretary*

Monthly Meeting, June 7, 1928

ACRODERMATITE SUPPURATIVE CONTINUE (HALLOPEAU). Presented by DR. MESTRE.

L. P., a white man, a Spaniard, aged 50, came to the hospital two and a half years before presentation, suffering from pustular lesions of both hands. These pustules had a tendency toward peripheral invasion, undermining the epidermis and constituting ringlike lesions. Smears from the pus and cultures in different culture mediums have repeatedly shown the absence of micro-organisms and of fungi. At present the palms and all the fingers are affected. The finger-nails have fallen off. The pustules are abundant, recurring on the red, atrophic, shiny skin, and the small joints of the hands had become ankylosed. Treatment had consisted of local applications of antiseptics, x-rays and ultraviolet rays, of intravenous injections of mercurochrome (220-soluble), of the administration of foreign bacterial proteins and arsenic and of autohemotherapy. Pathologic examination showed atrophy of the epidermis, lymphoid infiltration of the papillary layer with abscess formation and diffuse polynuclear infiltration.

PUSTULAR DERMATITIS HERPETIFORMIS. Presented by DR. QUERO.

J. C., a white woman, a Cuban, aged 26, married, had suffered from the condition for the past nine years before presentation. The lesions appeared in the form of recurrent attacks of pustular crops, accompanied by intense pruritus. At present, the patient is covered with papulopustular and crusted lesions of small size with herpes-like grouping, more abundant about the trunk. The blood count showed only 2 per cent of eosinophils, but in the seropurulent fluid of the lesions there were 8 per cent of eosinophils. The blood chemistry showed high uric acid (5.71 per cent).

DISCUSSION

DR. PELAEZ: I have used sulpharsphenamine in these cases with good results.

DR. MESTRE: I should like to know whether autohemotherapy has been used. I have treated patients who had dermatitis herpetiformis with injections of the contents of the vesicles, with apparently good results.

DR. SAENZ: In my experience, sulpharsphenamine has not influenced favorably any of my patients with Duhring's disease. I think that the improvement noted in some patients may be due to the natural course of the disease. I have seen improvement following the treatment suggested by Dr. Mestre, but unfortunately the vesicles are too small in this case.

PRURIGO FEROX. Presented by DR. GRAU, DR. FERRER and DR. PELAEZ.

A colored woman, aged 40, had suffered from the disease for the past four years. The lesions were pea-sized, hard, well limited and hemispheric papules of the color of normal black skin or slightly darker. Some of the lesions presented a small vesicle or crust in the center. They were distributed over the extremities and trunk, more abundantly on the abdomen and the dorsum. Pruritus was intense at all times. The blood and urine were normal.

DISCUSSION

DR. PARDO-CASTELLO: I saw a similar case some years ago in which all therapeutic measures were useless. Dr. Saenz also saw this case. The pathologic condition was that of chronic inflammation. In the case under discussion, I would advise x-ray treatment.

DR. CASTRO-PALOMINO: I have seen good results in some cases following the use of glandular extracts. I would advise investigation of the basal metabolism of this patient and the administration of pluriglandular extracts.

PRURIGO AND MORPHEA. Presented by DR. GRAU, DR. PELAEZ and DR. FERRER.

M. L., white, aged 7, had been suffering since the second year of life from an extremely itchy, papulovesicular, symmetrical eruption of the extremities. On the right forearm there was an oval plaque of about 5 by 3 inches, yellowish white, shiny and of the consistency of parchment. There was a violaceous ring composed of dilated capillaries on the border. The blood count was normal, except for a high percentage of eosinophils (12 per cent).

DISCUSSION

DR. QUERO: I agree with the diagnosis. I would advise electrolysis of the patch of morphea.

SYSTEMIC BLASTOMYCOSIS. Presented by DR. PARDO-CASTELLO.

A white girl, a Cuban, aged 14, whose parents were born in Syria, was in good health until six years before presentation, when she had suffered from diphtheria (?). Ulcerations had often appeared in the mouth since that time, and nodular lesions in the skin had succeeded each other almost constantly. These lesions rapidly underwent ulceration. The mucous ulcers had invaded the soft palate, the tongue, the cheeks, the nose and the upper lip, leaving atrophic and retracted scars. Twice she had been intubated because of lesions of the same character in the larynx. The nasal septum had been destroyed; the right knee presented an irregular ulcer covered with a crust; in the right buttock there was an oval, irregular, sanious ulcer, the result of a gummatous lesion. The tongue and cheeks showed several ulcerations of irregular outline, covered by false membranes. The general health of the patient was well preserved. The Wassermann reaction of the blood was negative; the blood count showed slight anemia. The sputum was negative for Koch's bacilli. Examinations of the blood and local secretions for tuberculosis, cutaneous diphtheria, Hansen bacilli, *Leishmania,* glanders bacilli and ameba had been negative repeatedly. Double contoured, large, unicellular organisms had been found in the ulcers and also in one of the nodules before ulceration. The patient refused a biopsy.

DISCUSSION

DR. SAENZ: I saw this case three years ago, when the patient had lesions in the mouth. The skin was not affected then, and my diagnosis was stomatitis ulcerosa. Dr. Pardo says that he had seen the case five years ago, and that he had made the diagnosis of stomatitis aphthosa. There was not the slightest indica-

tion of the real nature of the disorder. The case is extremely interesting, and the diagnosis seems proved by the finding of *Blastomyces* in the closed lesion. I would suggest the use of a compound solution of iodine intravenously, but this patient suffers from laryngeal attacks which might be aggravated by the intensive use of the iodides.

DR. QUERO: I agree with the diagnosis. I would suggest, in accord with the experience of Nicolle in the treatment of patients with aspergillosis, the use of methylthiomine chloride, U. S. P. in 2 per cent solution intravenously.

DR. PARDO-CASTELLO: I think that this case may be classified as a case of systemic blastomycosis with mucous and cutaneous lesions. The symptomatic complex is quite similar to that described by the South American investigators, especially by Escomel. It is cases of this type that have been formerly called espundia and uta in South America. The iodides in this case seem to have improved the patient, although it is too soon to say anything definite. I intend to employ antimony and potassium tartrate as advised by Escomel.

SYMMETRIC PALMAR AND PLANTAR KERATODERMA AND AINHUM. Presented by DR. PARDO-CASTELLO and DR. MESTRE.

A colored woman, a Cuban, aged 17, had typical yellowish hyperkeratosis of the palms and soles with hyperhidrosis. Both small toes presented a circular constrictive band which on the right side had almost severed the toe. On the left side the condition was less marked. The disease was hereditary. In three generations, there had been seven cases of the keratoderma, and three of these patients suffered from ainhum.

DISCUSSION

DR. PARDO-CASTELLO: The case is interesting because of the possible relation between keratoderma symmetrica and ainhum. The last mentioned condition has been attributed to leprosy, and has been considered as a form of circular scleroderma, but few cases have been reported in connection with palmar and plantar keratoderma. The sections will be shown at a future meeting.

TWO CASES OF LUPUS VULGARIS. Presented by DR. ROSELL.

The first patient, a colored girl, aged 14, for a year before presentation had suffered from a hypertrophic, frambesiform patch about the size of a filbert and several small, semitransparent nodules on the right ala of the nose. The second patient was a man, aged 47; a large patch of elevated lupus vulgaris about the size of a palm occurred on the left buttock and extended to the margin of the anus; it was of three years' duration. The cases were presented because of the rarity of lupus vulgaris in Cuba. In the second case, the late appearance in life is also unusual. In both cases, pathologic examination confirmed the diagnosis.

DISCUSSION

DR. SAENZ: I agree with the diagnosis. The sections are very good. I would recommend treatment by cross scarifications, especially in the first case, in which the best cosmetic results are desirable.

DR. PARDO-CASTELLO: In cases like these in which the condition covers a small surface, I have obtained good results with electrodesiccation. Cross-scarification has the disadvantage of requiring a long time to produce satisfactory results.

A CASE FOR DIAGNOSIS. Presented by DR. GRAU, DR. FERRER and DR. PELAEZ.

A white child, aged 5, about a year before presentation had had, on the right buttock, a deep-seated nodule which broke down and was followed by similar lesions in contiguous areas. These lesions, coalesced to form an irregular, granu-

lating, foul ulcer. The impression then was that of multiple syphilitic gummas. Six months later, the patient developed a swelling of the left leg with the appearance of a diffuse cellulitis. It rapidly broke down, constituting a large, irregular, suppurating ulcer, which now covers all the antero-external surface of the leg and measures 15 by 8 cm. The Wassermann reaction has been negative repeatedly. Fungi have not been isolated. Antisyphilitic treatment with mercury, bismuth and arsphenamine have not produced improvement.

DISCUSSION

DR. PARDO-CASTELLO: I have seen several cases of this type. All of these patients come from the region of Ciego de Avila. These cases were first reported as cases of leprosy by Dr. G. M. Caballero, who founded his diagnosis on the presence of acid-fast bacilli in the ulcers. I have also found these acid-fast bacilli in most of my cases, but I am not convinced that they are Hansen's. On the other hand, these cases do not behave like cases of leprosy. There are no other lesions that could be identified as manifestations of leprosy, and the patients finally get well spontaneously after two or three years, which would not occur if the condition were leprosy. I think it possible that, after all, the condition described in Africa under the name of Chappa, by Read, and later in Cuba by Dr. Guiteras, is present in the case under discussion. I would suggest that the presenters look for acid-fast bacilli deep in the lesions.

DR. SAENZ: I have seen these cases too and have found acid-fast bacilli, but I do not think that the condition is leprosy. I would suggest microscopic examination for *Leishmania.*

DR. FERRER: We have searched for acid-fast bacilli and for *Leishmania,* but have not been successful in finding them. We also thought of the possibility of chappa.

ERYTHEMA GYRATUM PERSTANTS. Presented by DR. SAENZ.

A policeman has had the condition in the form of erythematous, arciform, annular and serpiginous lesions for several months. They are situated on the trunk and extremities. A diagnosis of leprosy, drug eruption or syphilis has been ruled out.

MULTIPLE SARCOIDS OF BOECK. Presented by DR. RIO and DR. ROSELL.

A full-blooded negro, aged 50, presented on the epigastric and left costal regions and also on the arms, numerous nodular lesions varying in size from that of a pea to that of a filbert; these lesions were dark violaceous and deeply infiltrated. Injections of arsenic and a gold compound had caused most of them to undergo central involution, leaving atrophic, apigmented and violaceous scars. Sections showed the typical picture of sarcoid, with many giant cells.

DISCUSSION

DR. CASTRO-PALOMINO: When these patients do not respond well to therapy with gold compounds, it has been advised to use tuberculin. It seems that tuberculin sensitizes the patients, and they later improve satisfactorily under treatment with gold preparations.

A CASE FOR DIAGNOSIS. Presented by DR. GRAU, DR. FERRER and DR. PELAEZ.

The hands of a colored woman, aged 60, showed apigmented patches alternating irregularly with slate-colored lesions with well defined margins. The condition extended to the lower third of the forearm, and the symmetry was almost perfect. There was irregular palmar keratosis. Pruritus was intense. The patient said that the disease had been present for many years, and that its progress had been slow. Fungi had not been recovered.

DISCUSSION

DR. PARDO-CASTELLO: I have seen many of these cases, but have not made a satistactory diagnosis. Vitiligo is easily ruled out by the color and outline of the lesions. In the sections, I have seen a diffusion of the pigment in the upper layers of the corion. I had almost convinced myself that these cases could be identified with the disease described by Niuenhuis in Java under the name of "tinea albigena," although I was able to recover a fungus in only one case. At the last meeting of the American Dermatological Association, Dr. Howard Fox presented pictures of Colombian cases of "pinta," or "caraate," which struck me as being cases of exactly the same condition as that in the case presented, the only difference being that Fox did not observe the palmar and plantar hyperkeratosis. I call attention to this point, because up to the present we have not found "pinta" in Cuba.

DR. SAENZ: I would like to know whether Dr. Fox obtained cultures of fungi from his cases.

DR. PARDO-CASTELLO: He could obtain very few cultures in a considerable amount of material collected. It must be remembered that in these cases the disease is represented by the slate-colored, spreading margin, the achromic patches being secondary and entirely devoid of fungi. In a good many conditions, fungi are extremely difficult to find and to cultivate.

DR. GRAU: *Aspergillus* is hard to isolate and it is even more difficult to isolate many other fungi.

DR. SAENZ: I think that at least on direct examination the percentage of observations should be high if the fungi are really present.

PITYRIASIS LICHENOIDES CHRONICA (JULIUSBERG). Presented by DR. SAENZ.

A man, aged 45, had had the disease for the past ten years. He had been seen by numerous dermatologists in this city and abroad. The lesions were papular, pink or red and lentil-sized, especially on the palms, and resembled the lesions of secondary syphilis; on the trunk, a good many lesions had the appearance of pityriasis rosea. The patient had been refused many good positions because the diagnosis of active syphilis had often been made. Treatment has not been of any avail up to the present. Under treatment with injections of a gold preparation, the patient seemed to improve temporarily.

DISCUSSION

DR. PARDO-CASTELLO: I agree with the diagnosis. I would suggest treatment with ultraviolet light until a second degree dermatitis is produced.

V. PARDO-CASTELLO, M.D., *Recorder*

Monthly Meeting, July 12, 1928

FOLLICULITIS DECALVANS. Presented by DR. FERRER.

A Spaniard, aged 26 years, had noticed the condition of the skin for the first time about two years before presentation. The lesions consisted of follicular pustules, symmetrically situated in patches, on the thighs and legs. Healing took place by scar formation and consequently the hair failed to regrow. The legs were almost entirely devoid of hairs, in which place there were innumerable small, atrophic, punctiform scars. The surface of the skin in these locations presented a violaceous tint.

DISCUSSION

DR. PARDO-CASTELLO: I have seen a good many cases of this condition in hospital and private practice. The best results are obtained by x-ray depilation as used in sycosis.

DR. SAENZ: I wish to ask Dr. Pardo-Castello how long it takes to depilate one of these patients. I would suggest the use of autogenous vaccine.

DR. GRAU: One of our laboratory men is preparing an autogenous vaccine filtrate to use locally in cases of this kind, following Bedreska's ideas on local immunity. I have not had any personal experience.

DR. QUERO: I have seen patients with this type of disease successfully treated in Paris by Darier and Elliasheff with injections of 10 cc. of autogenous blood twice a week.

DR. PARDO-CASTELLO: I have used the vaccine filtrates in furunculosis and other pyogenic conditions, without results. Concerning the x-ray treatment, one epilating dose may be sufficient, but there are recurrences which may need further treatment.

SCLERODERMA AND SCLERODACTILIA. Presented by DR. GRAU, DR. FERRER and DR. PELAEZ.

A colored woman, aged 37 years, two years before presentation noticed cramps and coldness in her hands. Gradually the skin of the hands and arms had become hardened and tense, adherent to the subjacent tissues and cold to the touch. The fingers were thin and encased in the thickened skin. The nails were friable and thinned. The results of the examinations of the blood and urine were negative.

DISCUSSION

DR. QUERO: May I ask the treatment used?

DR. FERRER: We saw the patient for the first time about a week before presentation, and although we have given her doses of thyroid extract by mouth, we cannot say what the results will be.

DR. QUERO: I would use pluriglandular extracts.

HIRSUTIES PAPILLARIS PENIS (MAJOCCHI). Presented by DR. FERRER.

A young mulatto, in whom the negro blood predominated, had nearly 100 small papillary projections, from 1 to 3 mm. in length around the corona of the glans penis, which were regularly disposed in rows, whitish and gave the impression of small condylomas. The patient said that the condition had been present all his life and that the papillary projections had not grown in size or in number. A brother had the same condition. There were not any subjective symptoms.

DISCUSSION

DR. PARDO-CASTELLO: The condition is rather frequent in a smaller degree, but I must say that this is a most remarkable case. I have read the case published by Majocchi in the *Giornale di malattie della pelle*, but I doubt if any case could be more pronounced than this.

DR. FERRER: I have brought the case to your attention because of its considerable rarity and because of its possible confusion with condyloma acuminata. Majocchi has described this abnormality as a stigma of degeneration. It has been found in cats and anthropoid apes.

LATE HEREDITARY SYPHILIS OF THE BONES. Presented by DR. RIO.

A colored man, aged 32, a Cuban, single, was in a state of extreme emaciation. He came into the service with the diagnosis of tuberculosis of the skin. This man had been suffering from the present condition for the last twenty-five years,

the first symptoms having appeared when he was 7 years old, in the form of tumors and ulcers on both legs. On examination, both legs appeared deformed, curved in the classic, saber-blade shape, and there were numerous atrophic scars over both tibiae. On the right clavicle, toward its inner third, on the spinal column over the tenth vertebra, on the seventh right rib toward its middle and on the right olecranon, there were gummatous lesions, some of them showing discharging sinuses. Several whitish, irregular, atrophic scars were seen here and there on the trunk and extremities. There were typical Hutchinson's teeth and an abnormal implantation of the upper incisors. The Wassermann reaction was strongly positive; the Pirquet test was also positive and the blood count showed slight anemia. Examination of the lungs by a competent internist showed only diminution of the vesicular murmur over the apexes. Fluoroscopic examination of the lungs resulted in normal observations.

DISCUSSION

DR. PARDO-CASTELLO: This case is interesting because of the limitation of the lesions to the skeleton. The patient has never had any antisyphilitic treatment, having been considered as a case of tuberculosis. That tuberculosis is playing any rôle in this case is improbable. In my opinion, all the lesions are frankly due to syphilis. It is to be regretted that x-ray photographs have not been taken.

DR. SAENZ: This patient reminds me of the cases we saw and read about many years ago, when syphilis was still more difficult to control than it is today and when deep and destructive lesions were common. It would be interesting to know if the spinal fluid shows any alteration, after so many years of active syphilis without treatment.

DR. QUERO: I think that it has been practically demonstrated that extensive cases of cutaneous and osseus syphilis are always free from lesions of the nervous system. There seems to be a sort of vaccination of the central nervous system in these cases. Sezary has published a case similar to the one under discussion in which the spinal fluid was negative. He attributes this indemnity of the nervous system to a real vaccination on the skin that would protect the nervous system.

DR. CASTRO PALOMINO: In my opinion, cutaneous and other external lesions of syphilis do not mean the absence of syphilis of the nervous system. This has been widely discussed, and both Ravaut and Sezary are of this opinion.

DR. SAENZ: It is a well known fact that patients with cutaneous syphilis do not, as a rule, develop manifestations of the nervous system, but we have seen patients with hereditary syphilis with early cutaneous symptoms, who later have developed lesions of the nervous system.

DR. RIO: I wish to express my appreciation for the discussion. I am waiting to improve the precarious general health of the patient before I perform a spinal puncture. I shall be glad to report on the observations and on the result of the treatment at a future meeting.

A CASE FOR DIAGNOSIS. Presented by DR. PARDO-CASTELLO.

E. D., a white girl, aged 17 years, single, a Mexican, said that she had had the condition of the skin under investigation since January, 1927. On the nape of the neck, covering a surface of 8 by 6 cm., there was an irregular, slightly elevated, plaque of the color of cafe-au-lait, which did not produce any subjective sensations. On close examination, this plaque was composed of small papular lesions, flat topped, closely aggregated, with a mosaic-like arrangement which reminded one of lichenification. On the edges of the plaque there were several small, rounded, atrophic, superficial scars. On the abdomen, surrounding the umbilicus there was a similar plaque about 4 by 3 cm. On the bend of the left elbow, there were a few discrete, flat, yellowish papules, the size of a pinhead. There was not nor has there been any desquamation and the patient has not com-

plained of any subjective sensations at any time. Under fractional x-ray treatment, all the lesions practically disappeared, and after four months the patient was apparently cured. Two months before presentation, the condition reappeared in the neck and elbow, but not on the abdomen. The patient refused permission for a biopsy.

DISCUSSION

DR. SAENZ: The case is most unusual. I may suggest the possibility of this being a case of epidermodysplasia verruciformis of Lewandowsky, recently brought up by Gougerot who has described what I believe to be a variety of this condition. The disease is represented by small, coalescent, verrucous papules, grouped in patches, with a mosaic-like arrangement, as in lichenification, but without pruritus. The biopsy might help in the diagnosis.

DR. PARDO-CASTELLO: The patient has refused permission for biopsy. I do not think that this is a case of epidermodysplasia verruciformis of Lewandowsky. I was in favor of parapsoriasis lichenoides until the condition began to clear up under x-ray treatment.

LUPUS VULGARIS. Presented by DR. PELAEZ.

T. L., a colored man, aged 34 years, well built and muscular, came to the outpatient department of the Municipal Hospital to consult about a disease of the skin that had been in existence for the last six years. The patient had had syphilis ten years before presentation and had received adequate treatment. The present lesion was a small, slightly raised patch, 2 by 1 cm., situated in the inner third of the right eyebrow. It was dark red and in its center several yellowish points, deeply situated, could be seen. The sections confirmed the diagnosis of lupus vulgaris.

DISCUSSION

DR. SAENZ: I think that the diagnosis is correct. I would treat this patient with the fine point of the electrodesiccator.

DR. MESTRE: I would try the effect of gold salts in this case. It seems that lupus vulgaris does not respond well to this form of therapy, but due to the small surface affected, I think that it would be worthwhile to try.

DR. QUERO: Darier's creosote paste may be useful in this case. I have seen it used with startling success at Ravaut's clinic.

ERYTHEMA MULTIFORME. Presented by DR. MESTRE.

A white man, aged 48, unmarried, born in Cuba, noticed the first skin symptoms in 1926. Five months before presentation, the patient began to feel under par, had slight fever in the evenings and complained of rheumatic pains in the legs. At the same time the cutaneous lesions began to appear. On examination, both the upper and lower limbs and the gluteal regions were covered by small purpuric spots, small raised papules, small wheals, vesicles and vesicopapules, irregularly distributed. There was a certain amount of itching and vague articular pains. The blood pressure was 110 systolic and 65 diastolic (Vaquez); the results of the Wassermann and Kahn tests were negative; the coagulation time was ten minutes (Lee and White). The blood count was: red blood cells, 4,555,000; white blood cells, 8,000; polymorphonuclears, 55 per cent; lymphocytes, 30 per cent; mononuclears, 7.5 per cent, and eosinophils, 7.5 per cent. The results of the urinalysis were normal.

DISCUSSION

DR. CASTRO PALOMINO: I do not agree with the diagnosis of erythema multiforme. It seems to me that this is a case of purpura. Dr. Mestre described papular, urticarial and erythematous lesions which I have not seen today. It may be that the case has changed in the last few days. The patient must be kept under observation before deciding on the final diagnosis.

DR. SAENZ: Evidently this patient presents a symptomatic complex which is often difficult to individualize. The fact is that the patient has presented a polymorphous eruption, undoubtedly toxic or infectious, which is predominantly purpuric. It would be interesting to find out the platelet count and the retractibility of the blood clot.

DR. FERRER: I believe that clinically the diagnosis is purpura. From an etiologic point of view, I agree that purpura, urticaria and erythema multiforme are closely related.

DR. MESTRE: I had the opportunity of observing this patient for several days and can vouch for the existence of erythematous, papular and vesicular lesions. Even today, examination proves that the lesions are not purely purpuric. There is an inflammatory element in most of the lesions which is not due to the extravasation of blood. This is a clear example of how the toxic or toxi-infectious syndrome urticaria-erythema multiforme-purpura, may exist in the same person and may change from one type to another.

KRAUROSIS VULVA AND LEUKOPLAKIA. Presented by DR. ROSELL.

S. A., a white woman, married, aged 48 years, a Cuban, has suffered from pruritus of the vulva for the past sixteen years. There was a history of intermittent vaginal discharge. The patient was a small, withered woman who looked much older than the stated age. The vulva was atrophied, the labia majora were flattened and flabby, the labia minora had completely disappeared. On the mucous surface of the labia, the entrance of the vagina and the fourchet, there was a large, irregular, plaque of leukoplakia. On the left labium the leukoplakia formed a raised, grayish-white, papillomatous nodule, about 2 cm. in size. Sections of this nodule exhibited acanthosis, hyperkeratosis and round cell infiltration of the corium. There was not any malignancy.

DISCUSSION

DR. MESTRE: I agree with the diagnosis. The verrucous lesion on the left labium majus seems clinically an epithelioma. I think that radium or the electrodesiccator is indicated. I personally prefer the electrodesiccator, because it is easier to handle and healing takes place more quickly.

LICHEN PLANUS MONILIFORMIS. Presented by DR. PARDO-CASTELLO.

A white man, aged 46 years, born in Cuba, entered the skin ward of the Calixto Garcia Hospital, suffering from a large varicose ulcer of the right leg. On examination there was a papular, itchy eruption on both legs and arms. On the anterior aspect of both thighs there were gray, hard, flat papules, rough to the touch and regularly disposed in parallel lines. Individually these papules were from the size of a pinhead to that of a grain of sago, and on close inspection the surface appeared hyperkeratotic and somewhat scaly. In the lumbosacral region, there were patches of similar lesions much more flat and sparse, and toward the loins they resolved into a slight, dotty pigmentation. On the left leg there were large, rough, hyperkeratotic papules, also arranged in parallel rows like the beads of a rosary and of the same grayish color. In places, the lesions were frankly verrucous. Toward the internal aspects of the legs and thighs, the papules were dark red, flat and shiny, with a slight pityriasic desquamation. The mucous membrane of both cheeks showed patches of whitish, interlaced, flat papules. The condition had begun five years before on the left leg. There had been periods of improvement and new outbreaks from time to time. The lesions of the mouth were unknown to the patient. The Wassermann reaction was negative. The results of the urinalysis were negative.

DISCUSSION

DR. FERRER: I wish to call attention to the possibility of lesions of the type here shown on the leg, being due to the secondary changes which often occur

in inflammatory dermatosis, usually eczema. I have seen several cases of chronic eczema develop into a verrucous patch resembling an old lichen planus obtusus.

DR. SAENZ: I have the same opinion concerning the verrucous lesions of the leg, but in this case Dr. Pardo-Castello has shown us unmistakable manifestations of lichen planus of the mucous membrane of the mouth. The moniliform lesions of the legs and thighs are also typical of lichen planus of chronic evolution. The case is extremely rare.

EXTRAGENITAL SYPHILITIC CHANCRE. Presented by DR. MESTRE.

A white man, aged 24 years, born in Spain, fifteen days before presentation noticed a slight abraded surface on the right groin, just on the middle of the fold of Poupart's ligament. This abrasion enlarged until it reached the size of 4 by 2 cm., with a slightly indurated base and a red beefy surface. There was a generalized gland enlargement. *Spirochaeta pallida* were abundant on the secretion. The Wassermann reaction was strongly positive.

PITTSBURGH DERMATOLOGICAL SOCIETY

GEORGE J. BUSMAN, M.D., *Secretary*

Regular Meeting, June 21, 1928

L. G. BEINHAUER, M.D., *Chairman, Presiding*

SECONDARY SYPHILIS—LATE RECURRENT TYPE. Presented by DR. SCHWARTZ and DR. BUSMAN.

L. F., a man, aged 47, single, an American, presented a generalized, superficial, erosive condition covering the nasopharynx and the soft palate. The entire area was covered with a white desquamating pellicle which bled easily when disturbed. The trunk, upper arms and legs were covered with a faint but distinctly evident roseola. The infiltrated macules varied in size from that of a split pea to 2 cm. in diameter. There was no evidence whatever of a primary sore of recent date. Dark-field examination of secretion from the lesion of the mucous membrane showed a few typical *Spirochaeta pallida.* Neither spirochete of Vincent's angina nor fusiform bacilli were present.

This patient had had a penile sore in 1917, which was diagnosed as primary syphilis; the lesion disappeared promptly following a single injection of old arsphenamine. He had not had any treatment since. The present sore throat had been somewhat transient in severity, but continually present for the past seven months. This case illustrates the possibilities of transmission in the late mucous membrane and skin recurrences.

DISCUSSION

DR. HOLLANDER: The coexistence of syphilis and carcinoma of the buccal mucous membrane is so frequent that calling attention to it seems unnecessary. I think we are all at a disadvantage in making a diagnosis because the lesions on the abdomen are not characteristic for a secondary syphilitic exanthema.

DR. CRAWFORD: The lesion in the pharynx impresses me as a carcinoma. It is sharply marginated and bleeds easily.

DR. GUY: I feel that it is not proper to call any spirochete from the oral cavity *Spirochaeta pallida.* Other types found there too closely simulate this organism to make a morphologic differentiation satisfactory. A hidden primary, as intrarectal lesion, should be ruled out.

NOTE.—The lesions of the mouth and the cutaneous lesions in this case had completely healed at the end of one week following his first treatment with arsphenamine.

SUBUNGUAL ANGIOMA AND ECTASIA LIMITED TO THE HANDS AND TONGUE. Presented by DR. GUY and DR. JACOB.

P. T., a colored woman, aged 41, presented lesions of the finger-nails and hands. The right hand showed two nails having a detached scaly bed, while the left hand presented an ulcer under one nail, of two years' duration, and a hemorrhagic spot under another nail. The patient gave a history of frequent hemorrhage from the ulcer when slightly injured. There were similar lesions on the tongue.

DISCUSSION

DR. CRAWFORD: I would consider this case as one of congenital telangiectasia.

DR. HOLLANDER: The question of syphilis must be considered, and from that standpoint the case is of great interest.

DR. GUY: The reason the case was presented under the title given was that a familial tendency was not obtained in the history and other types, notably syphilis, had not been ruled out.

ACANTHOSIS NIGRICANS (JUVENILE TYPE). Presented by DR. WERTHEIMER.

J. C., a girl, aged 16, presented grayish, thickened, wartylike areas, in both axillae extending slightly onto the sides of the chest, for at least four years. On the back of the neck at the folds, there was a brownish pigmentation with hyperkeratotic lesions. On the abdomen, the sides of the chest and the regions of the groin there were various sized, pigmented areas varying from light to dark brown. The patient was obese and alert, yet gave one the impression of having an endocrine disturbance. She was 5 feet 1½ inches (156.27 cm.) tall and weighed 184¼ pounds (83.6 Kg.). The menses were normal, but irregular. One year before presentation she received three roentgen-ray treatments at which time the physician thought he noticed some slight improvement.

DISCUSSION

DR. CRAWFORD: I agree with the diagnosis.

DR. GUY: I agree with the diagnosis. Being of the juvenile type, the prognosis is better than with the adult.

DR. HOLLANDER: The only eruption similar to this which I have seen has been in patients using face preparations containing mercury or lead.

PRURIGO NODULARIS. Presented by DR. PHILLIPS.

E. R., a woman, a housewife, aged 36, presented lesions of ten years' duration. The lesions were firm, and nodular; they were verrucous and varied in size from that of a pea to that of a thumbnail. They were found on the hands and arms extending to the shoulders, also on the feet, legs and thighs, stopping at the hips. Some of the lesions showed excoriations and hemorrhage, and in some places two or three small lesions had coalesced to form a plaque.

The patient complained of intense itching. New lesions occasionally appeared but none of the lesions had disappeared so far as the patient knew, after they had become established. The family and personal history were negative except for an eclampsia which had terminated her only pregnancy, during the past winter.

Treatment with roetgen ray, arsenic and local applications had not been of any avail.

In all, this patient had about 180 lesions.

PELLAGRA (ALCOHOL). Presented by DR. BEINHAUER.

W. M., a man, aged 31, single, presented himself for examination four weeks ago complaining of diarrhea, weakness and an eruption of the skin involving the hands, face and neck. The past history was negative except for constant alcoholism (moonshine drinking) for the past four to six years. The present condition began six weeks before presentation, following a "moonshine debauch" when the patient first noticed a severe diarrhea (from sixteen to twenty-four movements daily) and a sore mouth together with a marked weakness, cramping pains in the legs, marked fatigue and nervous irritability, together with loss of weight (from 15 to 20 pounds [from 6.8 to 9 Kg.] in two weeks). During the debauch, the patient abstained from food. Examination revealed a young man, extremely irritable, weak and somewhat disoriented. The facial expression was typically anxious. The sclera of the eyes was markedly jaundiced. The tongue was beefy red, erosive and painful to the touch, with congested mucous membrane and apthous ulcerations along the border of the lip and the frenum of the tongue. The face and neck presented a pigmented, reddish brown, desquamating "sunburn"-like appearance. Symmetrically involving both hands and limited to the dorsum, there was an acute vesiculoscaly, painful, sharply glovelike, defined eruption not unlike an ultraviolet ray dermatitis. The palms were free. Except for the exposed portions of the body, the skin was normal in appearance. The reflexes were exaggerated, and the patient presented a definite tremor in both hands. Marked tenderness was elicited over the large nerve trunks. The abdomen was distended with areas of tenderness over the border of the liver and the descending colon. The Wassermann reaction of the blood and the urinalysis were negative. The blood picture revealed a secondary anemia and a leukocytosis.

The patient was put to bed at absolute rest with the complete withdrawal of alcohol. Fluids were forced and diarrhea was controlled by the use of bismuth and paregoric. The diet consisted entirely of fresh fruit juices and a vegetable diet with cod liver oil, with three hour feedings. Locally, mild antiseptic ointment was applied. The present condition still reveals a pigmentary reaction, two weeks after discharge from the hospital.

LICHEN PLANUS ATROPHICUS ET SCLEROSIS (?). Presented by DR. HOLLANDER.

T. K., a colored man, aged 34, married, presented a disseminated eruption on the face, neck, penis, rectum and mouth. The lesions varied in appearance; some were flat with a central thinning, and some were hypertrophic and papular. On the glans penis, there was a single papule, which was shiny and carried the character of lichen. The right side of the buccal mucous membrane was grayish. The first lesion was of two years' duration, progressive and at times extremely itchy.

DISCUSSION

DR. BUSMAN: This case impresses me more as a tuberculosis of the skin. It is similar to the case presented by Dr. Norris last year, which at that time was considered as lichen planus or syphilis. A biopsy showed the condition to be tuberculosis.

At the Cleveland Annual Meeting, this patient was again presented and his condition was generally agreed to be tuberculosis in view of the supporting biopsy.

DR. HOLLANDER: The presence of the grayish membrane in the mouth and the single papule typical of lichen planus on the glans penis made me favor the diagnosis of lichen planus although the question of tuberculosis of the skin must be ruled out. A biopsy report will be given.

ERYTHEMA MULTIFORME COMPLICATING ECZEMATOID DERMATITIS. Presented by DR. GUY and DR. JACOB.

A man, aged 74, had been under our care for an eczematoid dermatitis of the right leg, which originated from a discharging sinus, which in turn was the result of a compound fracture of the tibia. About the time the sinus healed over and the

eczematoid dermatitis was under control, the present condition appeared. Large bullae were present principally on the fractured leg below the knee. On the forearms, the neck and the other leg, there were macular and papular, variously sized and shaped, erythematous lesions which appeared about twenty-four hours after the bullous eruption on the fractured leg.

DISCUSSION

DR. GUY: The case was of interest in that it demonstrated the effect of trophic disturbance on the fractured leg in producing a different type of eruption from that seen elsewhere. The case was also of interest in that it seemed fair to assume that the erythema multiforme was of infectious origin in view of the history.

NOTE.—Subsequent examination revealed a fungus in the roof of the bullae, and the condition was clearing under treatment for dermatophytosis.

RADIODERMATITIS. Presented by DR. HOLLANDER.

V. M., a woman, aged 45, presented a healing ulceration as a result of an x-ray burn, above the sternoclavicular junction in the central area. Seventeen years before presentation, the patient had been given x-ray treatments for a cyst in this location. These treatments were repeated at various intervals since then. One year before presentation, the skin began to break down, and when first seen, on Nov. 30, 1927, the entire area which was healed, was ulcerating, foul-smelling and extremely painful, and bled readily with the slightest trauma.

The patient was presented to show the effect of wax dressings as a means of temporary relief.

DISCUSSION

DR. GUY: I am interested in the therapy and would like to see the end-result. I feel that, if possible, excision and graft would be the method of choice and would save much time and suffering.

DR. HOLLANDER: This was simply a temporary dressing, which cleared up a foul-smelling, ulcerating radiodermatitis and will be followed by excision with a radio knife, at least for a biopsy. I do not consider this a permanent cure of the condition by any means.

DR. PHILLIPS: I believe that a biopsy with cautery or the radio knife should be done and the treatment based on the microscopic observations.

BROMODERMA. Presented by DR. GUY and DR. JACOB.

A school teacher, aged 20, presented a nodular granulomatous eruption of the chin of eight months' duration. The patient had been under treatment for carbuncle during the past seven months. She had been taking a bromide mixture off and on for one year. Bromine was demonstrated in the urine by the fluorescein test. The patient had received 80 cc. of physiologic solution of sodium chloride and a fractional application of x-ray.

PEMPHIGUS VULGARIS. Presented by DR. HOLLANDER.

A. R., a woman, aged 54, unmarried, was presented to show the effect of whole blood transfusions, feeding of liver extract and high colonic irrigation with sulphonated bitumen, N. F. In September, 1927, this patient was referred to my service at Mayview, by Dr. Guy. At that time the entire body was covered with flaccid, bullous lesions. Its contents changed rapidly from a serous to a purulent type. The patient was extremely weak and to all appearances was moribund. By constant repetition of transfusion at weekly intervals, of large quantities of whole blood (500 to 1,000 cc.) I have been able to clear the patient to the extent which you can see this evening. On Jan. 1, 1928, I began to use liver extract and daily high colonic irrigations with sulphonated bitumen, N. F. The patient seems to

be improving steadily. She is able to be up and around, and, except for intense itching which has been ameliorated within the last two weeks by larger blood transfusions, she seems more comfortable.

DISCUSSION

DR. HOLLANDER: The improvement was so marked that I feel the presentation was of value to further prove that whole blood transfusion has a definite place in the therapy of pemphigus.

DR. GOLDMAN: I saw the patient at the same time that Dr. Hollander first saw her, and at that time the picture was that of a typical pemphigus vulgaris. She had large bullae such as I have never seen in Duhring's disease.

DR. GUY: Dr. Hollander's case as originally seen was a typical pemphigus vulgaris rapidly progressive with flaccid bullae generalized, including the oral and vaginal mucosa. It was interesting to note the remarkable improvement and the change in character of the eruption simulating a dermatitis herpetiformis with intense itching, which latter was entirely absent.

Book Reviews

SYPHILIS. By CHARLES C. DENNIE, M.D. Price, $2.50. Pp. 304. New York: Harper & Brothers, 1928.

Dr. Dennie's object in this work has been to write a practical book as compact as possible but covering the entire subject of syphilis. It is a difficult undertaking, but it may be said at once that the book is excellent. His style is clear and direct, and his teaching is sound. He uses some striking phrases, as when speaking of the lack of tissue reaction in the early days of the invasion of the spirochete he says: "A few leukocytes make their appearance, but they seem to be on friendly terms with the invading parasite."

Some of his usage does not appeal to the reviewer. Instead of the term hereditary syphilis, he uses throughout the book, not as a compound word but as two words, that horrible phrase heredo syphilis. He chooses also to use *Treponema pallidum* instead of *Spirochaeta pallida*. The selection of words depends on good usage, and good usage has determined the adoption of *Spirochaeta pallida*, so that it is hopeless to try to replace it. *Treponema pallidum* is like spats, favored by a few of the meticulous.

There are two or three clinical pictures in the book and only a few others, all of which illustrate technical procedures.

Dr. Dennie has done a service in writing this book. It is the first of a series of monographs which are to be published by Harper & Brothers on various subjects in medicine. This evidence of active participation in the publication of medical books by the old firm of Harper & Brothers is welcome. The reviewer is particularly glad that they are making their new entry in this field by the publication of a series of monographs, and hopes that some of them may deal with less comprehensive topics than the whole subject of syphilis.

One thing to be seriously criticized is that the book lacks an index. This is unpardonable in an extensive book that is worth publishing, and it is hoped that in future works of the series this defect will be remedied.

HANDBUCH DER HAUT-UND GESCHLECHTSKRANKHEITEN. Edited by J. JADASSOHN with many collaborators. Volume 15, part 1. Morphologie und Biologie der Spirochaeta Pallida; Experimentelle Syphilis. Bearbeitet von Erich Hoffmann, Edmund Hofmann, Paul Mulzer. Price, 90 R.M. Pp. 432, with 272 illustrations. Berlin: Julius Springer, 1927.

We are glad to welcome another volume of this monumental work. This volume, part 1 of volume 15, is devoted to the morphology and biology of *Spirochaeta pallida* and to experimental syphilis. Part 2 of this volume will deal with the etiology and general pathology of syphilis. The completeness with which the subject is covered is indicated by the extent of its consideration. To morphology and biology are given 115 pages; to experimental syphilis, 285 pages. The literature on the morphology and biology of *Spirochaeta pallida* occupies twenty closely printed pages; the literature on experimental syphilis occupies twelve pages. The subject of *Spirochaeta pallida* is handled by Prof. Erich Hoffmann of Bonn and Docent Edmund Hofmann of Frankfort. The selection of these men, especially Erich Hoffmann, is particularly desirable, because Erich Hoffmann of all men is entitled to write on this subject. His part begins with a fascinating history leading up to and including the discovery of *Spirochaeta pallida* and includes chapters on the structure, the life cycle and the modification of *Spirochaeta pallida* through chemical and physical agents. Then comes a chapter on classification and nomenclature. This is followed by chapters on methods of examination, on the cultivation and finally on the meaning of *Spirochaeta pallida* in diagnosis, prognosis and treatment. It may be noted, in passing, that Hoffmann

accepts as fixed in the literature and uses the term, *Spirochaeta pallida*. No one could write with more authority on experimental syphilis than Professor Mulzer of Hamburg. His work is too extensive to enumerate the chapters, but they cover every aspect of the subject of experimental syphilis.

One can only continue to express his admiration for the completeness and scholarly character of the system as a whole, as far as published.

DIE EINWIRKUNG VON KRANKHEITEN AUF DAS KOPFHAAR DES MENSCHEN. By PROF. DR. FELIX PINKUS. Price, 13 marks. Pp. 196. Berlin: S. Karger, 1928.

By this work Pinkus places us still further in his debt for his studies of the diseases of the hair and nails. The work is divided into three parts. The first part treats of the anatomy of the hair, the second part of malformation of the hair and the third part of change in the hair following disease. It is hard to think of anything under these headings which he has not included. It is a useful addition to the literature on the subject.

DIE HAUTKRANKHEITEN, LEITFADEN FÜR STUDIERENDE UND AERZTE. By KARL HERXHEIMER and EDMUND HOFMANN. Price, 13 marks. Pp. 270. Berlin: S. Karger, 1928.

This introduction to dermatology is one of the elementary treatises on the subject which our German colleagues know so well how to produce. A sound statement of the principles and important facts of the entire subject of dermatology is given. It is an excellent introduction to the subject, well arranged, clearly written and well balanced.

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Index to Current Literature

DERMATOLOGY

Chickenpox Immunization. K. von Késmárszky, Arch. f. Kinderh. **85**:1 (Aug. 31) 1928.

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CONTENTS

Multiple Superficial Benign Epithelioma of the Skin: Its Differentiation from Hereditary and Similar Eruptions. Fred Wise, M.D., New York 17

Skin Diseases of Endocrine Origin (Otherwise Dermal Neurosis, Poikiloderma Like Lues) Occurring in Connection with Undervelopment of the Sexual Glands and Disturbance of Adiposogenitalis. Walter Block, M.D., and H. Stauffer, M.D., Zurich, Switzerland 22

Lipid Studies in Xanthoma. Ulric Wile, M.D., Henry C. Eichhorn, Ph.D., and Arthur C. Curtis, M.D., Ann Arbor, Mich. 35

Experimental Studies in Eczema: III. The Rôle of the Sympathetic Nervous System and Calcium-Potassium Ratio in Altering Cutaneous Irritability to the Rabbit. Joseph V. Klauder, M.D., and Herman Brown, B.S., Philadelphia 52

The Occurrence of Tuberculoid Reactions in the Inguinal Glands in Early Syphilis. H. Gideon Wilkinson, M.D., with the Technical Collaboration of Edith Kersten, M.D., Minneapolis 62

Dermatitis Vegetans: Report of Two Cases of the Hallopeau Type. H. J. E. Wallhausser, M.D., Newark, N. J. 77

Jean Louis Alibert. Douglass M. Montgomery, M.D., San Francisco 87

The Hematogenous Production of Dermatomycoses: Experimental Studies. S. M. Peshkin, M.D., and M. B. Segal, M.D., Moscow, United Socialistic Soviet Republics 98

Mercuric Salicylate: A Study of Its Reaction in the Treatment of Syphilis. H. N. Cole, M.D., John Gamble, M.D., Nora E. Schreiber, A.B., and Torald Sollmann, M.D., Cleveland 105

Abstracts from Current Literature 119

Society Transactions:

New York Academy of Medicine, Section on Dermatology and Syphilis 125

Philadelphia Dermatological Society 131

New York Dermatological Society 133

Chicago Dermatological Society 142

Cleveland Dermatological Society 148

Cuba Dermatological Association 152

Pittsburgh Dermatological Society 161

Book Reviews 166

Directory of Dermatologic Societies 168

Index to Current Literature 171